Inventor Search

=> d l13 ibib abs hitstr 1-9

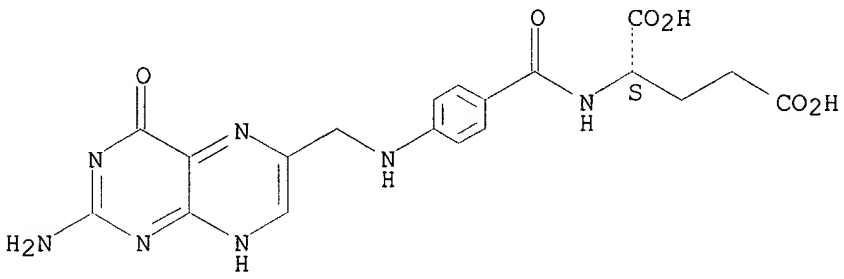
L13 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:77429 HCAPLUS
DOCUMENT NUMBER: 136:139833
TITLE: Drug **conjugates** containing dicarboxy C1-3 alkyldextran polyalcohols
INVENTOR(S): **Inoue, Kazuhiro**; Suzaki, Hiroshi
PATENT ASSIGNEE(S): Daiichi Seiyaku Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002030002	A2	20020129	JP 2000-215919	20000717

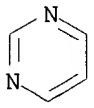
AB The invention relates to a drug **conjugate** wherein a dicarboxy C1-3 alkyldextran polyalc. is bonded to the residue of a medicinal compd., e.g. an antitumor agent and an antiinflammatory agent, with/without of a spacer consisting of one amino acid or a spacer consisting of 2-8 amino acids bonded to each other via peptide bonds. The **conjugate** exhibits excellent drug targeting property. **Dextran** polyalc. was reacted with diethylbromomalonate in the presence of cesium hydroxide to obtain dicarboxymethyl **dextran** polyalc. sodium salt. Cisplatin was reacted with AgNO3 and then, with the obtained dicarboxymethyl **dextran** polyalc. sodium salt. to make a **conjugate**. The **conjugate** showed sustained-release of low-mol.wt. Pt compd. in phosphate buffer.

IT **59-30-3**, Folic acid, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; drug **conjugates** contg. dicarboxy C1-3 alkyldextran polyalcs.)
RN 59-30-3 HCAPLUS
CN L-Glutamic acid, N-[4-[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



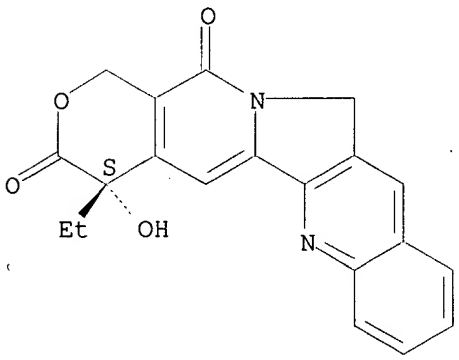
IT **289-95-2D**, Pyrimidine, fluoro derivs., **conjugates** with dicarboxyalkyl **dextran** polyalcs.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor agents; drug **conjugates** contg. dicarboxy C1-3 alkyldextran polyalcs.)
RN 289-95-2 HCAPLUS
CN Pyrimidine (8CI, 9CI) (CA INDEX NAME)



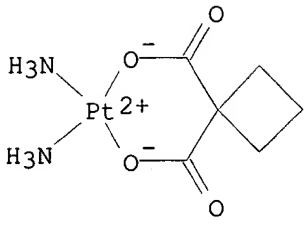
IT **9004-54-0DP, Dextran**, polyalcs., dicarboxymethyl derivs., **conjugates** with antitumor agents or antiinflammatory agents with/without of peptide spacers, biological studies
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug **conjugates** contg. dicarboxy C1-3 alkyldextran polyalcs.)
RN 9004-54-0 HCAPLUS
CN Dextran (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **7689-03-4D**, Camptothecin, derivs., **conjugates** with dicarboxyalkyl **dextran** polyalcs. **41575-94-4D**, Carboplatin, **conjugates** with dicarboxyalkyl **dextran** polyalcs. **61825-94-3D**, Oxaliplatin, **conjugates** with dicarboxyalkyl **dextran** polyalcs.
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug **conjugates** contg. dicarboxy C1-3 alkyldextran polyalcs.)
RN 7689-03-4 HCAPLUS
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4-ethyl-4-hydroxy-, (4S)- (9CI) (CA INDEX NAME)

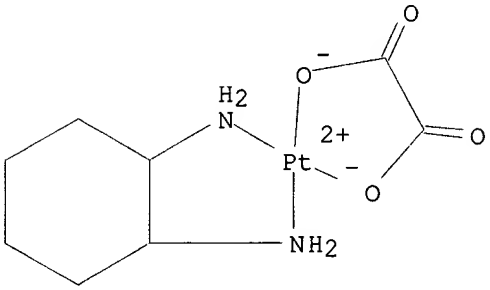
Absolute stereochemistry. Rotation (+).



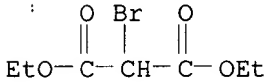
RN 41575-94-4 HCAPLUS
CN Platinum, diammine[1,1-cyclobutanedi(carboxylato-.kappa.O)(2-)]-, (SP-4-2)- (9CI) (CA INDEX NAME)



RN 61825-94-3 HCAPLUS
CN Platinum, [(1R,2R)-1,2-cyclohexanediamine-.kappa.N,.kappa.N'][ethanedioato (2-)-.kappa.O1,.kappa.O2]-, (SP-4-2)- (9CI) (CA INDEX NAME)

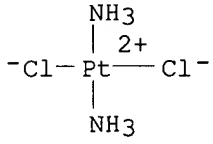


IT **685-87-0**, Diethylbromomalonate **9004-54-0**, **Dextran** T500, reactions **15663-27-1**, Cisplatin **84275-35-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of drug **conjugates** contg. dicarboxy C1-3 alkyldextran polyalcs.)
RN 685-87-0 HCAPLUS
CN Propanedioic acid, bromo-, diethyl ester (9CI) (CA INDEX NAME)



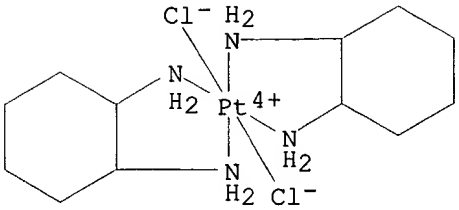
RN 9004-54-0 HCAPLUS
CN Dextran (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 15663-27-1 HCAPLUS
CN Platinum, diamminedichloro-, (SP-4-2)- (9CI) (CA INDEX NAME)

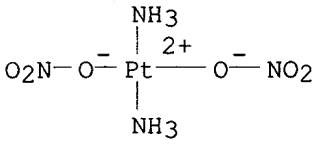


RN 84275-35-4 HCAPLUS
CN Platinum(2+), dichlorobis[rel-(1R,2S)-1,2-cyclohexanediamine-

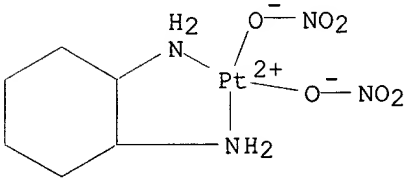
.kappa.N,.kappa.N']-, (OC-6-13)- (9CI) (CA INDEX NAME)



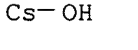
IT **41575-87-5P 60732-70-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of drug **conjugates** contg. dicarboxy C1-3 alkyldextran polyalcs.)
RN 41575-87-5 HCAPLUS
CN Platinum, diamminebis(nitrato-.kappa.O)-, (SP-4-2)- (9CI) (CA INDEX NAME)



RN 60732-70-9 HCAPLUS
CN Platinum, (trans-1,2-cyclohexanediamine-.kappa.N,.kappa.N')bis(nitrato-.kappa.O)-, (SP-4-2)- (9CI) (CA INDEX NAME)

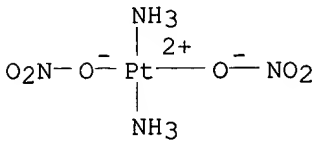


IT **21351-79-1**, Cesium hydroxide
RL: RGT (Reagent); RACT (Reactant or reagent)
(prepn. of drug **conjugates** contg. dicarboxy C1-3 alkyldextran polyalcs.)
RN 21351-79-1 HCAPLUS
CN Cesium hydroxide (Cs(OH)) (9CI) (CA INDEX NAME)

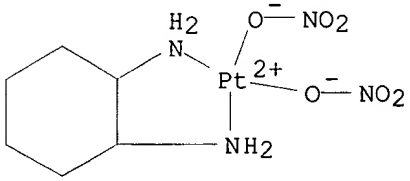


IT **41575-87-5DP, conjugates** with dicarboxymethyl **dextran** polyalcs. **60732-70-9DP, conjugates** with dicarboxymethyldextranpolyalc.
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of drug **conjugates** contg. dicarboxy C1-3 alkyldextran

polyalcs.)
RN 41575-87-5 HCAPLUS
CN Platinum, diamminebis(nitrato-.kappa.O)-, (SP-4-2)- (9CI) (CA INDEX NAME)

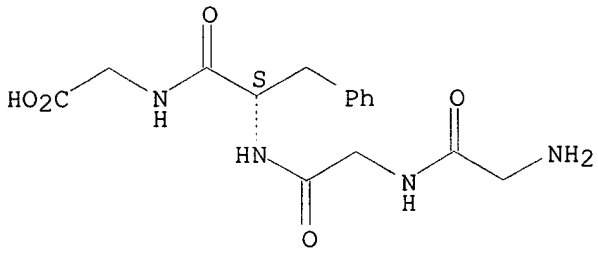


RN 60732-70-9 HCAPLUS
CN Platinum, (trans-1,2-cyclohexanediamine-.kappa.N,.kappa.N')bis(nitrato-.kappa.O)-, (SP-4-2)- (9CI) (CA INDEX NAME)



IT **200427-88-9DP, conjugates** with dicarboxymethyl **dextran** polyalcs. and antitumor or antiinflammatory drugs
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of drug **conjugates** contg. dicarboxy C1-3 alkyldextran polyalcs. and peptide spacers)
RN 200427-88-9 HCAPLUS
CN Glycine, glycylglycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L13 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:322648 HCAPLUS
DOCUMENT NUMBER: 135:185307
TITLE: Characteristics of tissue distribution of various polysaccharides as drug carriers: influences of molecular weight and anionic charge on tumor targeting
AUTHOR(S): Sugahara, Shuichi; Okuno, Satoshi; Yano, Toshiro; Hamana, Hiroshi; **Inoue, Kazuhiro**
CORPORATE SOURCE: Drug Delivery System Institute, Ltd., Chiba, 278-0022, Japan
SOURCE: Biological & Pharmaceutical Bulletin (2001), 24(5),

535-543
CODEN: BPBLEO; ISSN: 0918-6158
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Using the Walker 256 model for carcinosarcoma-bearing rats, we i.v. administered 5 **polysaccharide** carriers with various mol. wts. (MWs) and elec. charges and tested for their plasma and tissue distribution. Two carriers, carboxymethylated-D-manno-D-glucan (CMMG) and CMdextran (CMDex), showed higher plasma AUC than the other carriers tested, namely, CMchitin (CMCh), N-desulfated N-acetylated heparin (DSH), and hyaluronic acid (HA). This was consistently found to be true over the range of MWs tested. For CMDex, the max. value of plasma AUC was obtained when the MW exceeded 150 kDa. As for the anionic charge, CMDex (110-180 kDa) with a degree of substitution (DS) of the CM groups ranging from 0.2 to 0.6, showed max. plasma AUC values. Twenty-four hours after administration, the concn. of CMDex (180-250 kDa; DS: 0.6-1.2) in tumors was more than 3% of dose/g-approx. 10-fold higher than those obsd. with CMCh, DSH and HA. Doxorubicin (DXR) was bound to these carriers via a peptide spacer, GlyGlyPheGly (GGFG), to give carrier-GGFG-DXR **conjugates** (DXR content: 4.2-7.0 (wt./wt.)%), and the antitumor effects of these **conjugates** were tested with Walker 256 carcinosarcoma-bearing rats by monitoring the tumor wts. after a single i.v. injection. Compared with free DXR, CMDex-GGFG-DXR and CMMG-GGFG-DXR **conjugates** significantly suppressed tumor growth, while the CMCh-GGFG-DXR, DSH-GGFG-DXR, and HA-GGFG-DXR **conjugates** in a similar comparison showed weak tumor growth inhibition. These findings suggest that the antitumor effect of the carrier-DXR **conjugates** was related to the extent with which the carriers accumulated in the tumors.

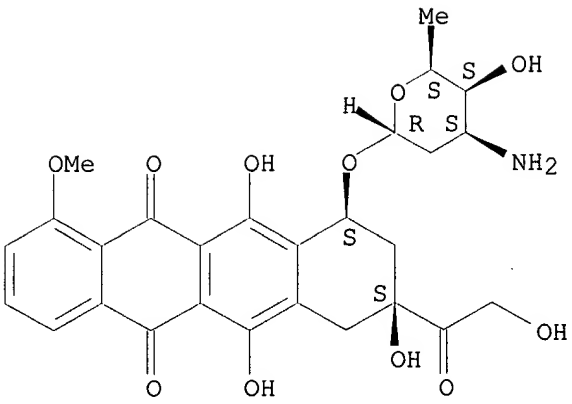
IT **9067-32-7DP**, Hyaluronic acid sodium salt, **conjugates** with doxorubicin and peptide **23214-92-8DP**, Doxorubicin, **conjugates** with peptide and polysaccharides **39422-83-8DP**, Carboxymethyl **dextran** sodium salt, **conjugates** with doxorubicin and peptide **65667-26-7DP**, **conjugates** with doxorubicin and peptide **105156-94-3DP**, Carboxymethyl chitin sodium salt, **conjugates** with doxorubicin and peptide **200427-88-9DP**, **conjugates** with doxorubicin and polysaccharides **355129-33-8DP**, **conjugates** with doxorubicin and peptide
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(effects of mol. wt. and anionic charge of **polysaccharide** drug carriers on tumor targeting)

RN 9067-32-7 HCAPLUS
CN Hyaluronic acid, sodium salt (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 23214-92-8 HCAPLUS
CN 5,12-Naphthacenedione, 10-[(3-amino-2,3,6-trideoxy-.alpha.-L-lyxo-hexopyranosyl)oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 39422-83-8 HCAPLUS
CN Dextran, carboxymethyl ether, sodium salt (9CI) (CA INDEX NAME)

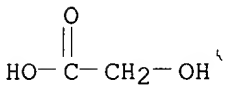
CM 1

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 79-14-1
CMF C2 H4 O3



RN 65667-26-7 HCAPLUS
CN Heparamine, N-acetyl, sodium salt (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 105156-94-3 HCAPLUS
CN Chitin, carboxymethyl ether, sodium salt (9CI) (CA INDEX NAME)

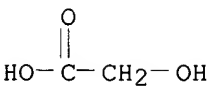
CM 1

CRN 1398-61-4
CMF Unspecified
CCI MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

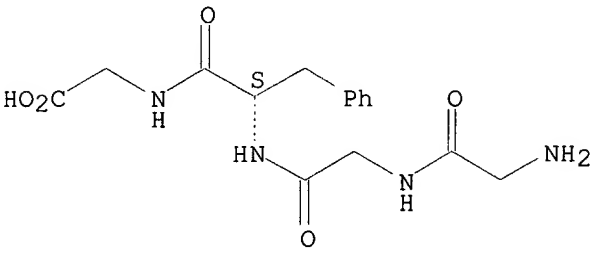
CM 2

CRN 79-14-1
CMF C2 H4 O3



RN 200427-88-9 HCAPLUS
CN Glycine, glycylglycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 355129-33-8 HCAPLUS
CN D-Gluco-D-mannan, carboxymethyl ether, sodium salt (9CI) (CA INDEX NAME)

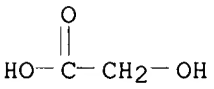
CM 1

CRN 11078-31-2
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 79-14-1
CMF C2 H4 O3



IT **9067-32-7P**, Hyaluronic acid sodium salt **39422-83-8P**,
Carboxymethyl **dextran** sodium salt **65667-26-7P**
105156-94-3P, Carboxymethyl chitin sodium salt
355129-33-8P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(effects of mol. wt. and anionic charge of **polysaccharide** drug carriers on tumor targeting)
RN 9067-32-7 HCAPLUS
CN Hyaluronic acid, sodium salt (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 39422-83-8 HCAPLUS
CN Dextran, carboxymethyl ether, sodium salt (9CI) (CA INDEX NAME)

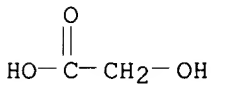
CM 1

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 79-14-1
CMF C2 H4 O3



RN 65667-26-7 HCAPLUS
CN Heparamine, N-acetyl, sodium salt (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 105156-94-3 HCAPLUS
CN Chitin, carboxymethyl ether, sodium salt (9CI) (CA INDEX NAME)

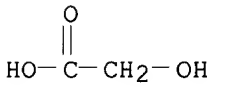
CM 1

CRN 1398-61-4
CMF Unspecified
CCI MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 79-14-1
CMF C2 H4 O3



RN 355129-33-8 HCAPLUS
CN D-Gluco-D-mannan, carboxymethyl ether, sodium salt (9CI) (CA INDEX NAME)

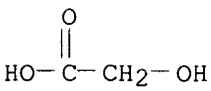
CM 1

CRN 11078-31-2
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 79-14-1
CMF C2 H4 O3



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:314580 HCAPLUS
DOCUMENT NUMBER: 132:326152
TITLE: DDS compounds and method for assaying the same
INVENTOR(S): **Susaki, Hiroshi; Inoue, Kazuhiro; Kuga, Hiroshi; Ikeda, Masahiro; Shiose, Yoshinobu; Korenaga, Hiroshi**
PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000025825	A1	20000511	WO 1999-JP6016	19991029
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9964880	A1	20000522	AU 1999-64880	19991029
BR 9915198	A	20010814	BR 1999-15198	19991029
EP 1155702	A1	20011121	EP 1999-952805	19991029
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 2001002128	A	20010620	NO 2001-2128	20010430

PRIORITY APPLN. INFO.:
JP 1998-310130 A 19981030
JP 1998-329272 A 19981119
WO 1999-JP6016 W 19991029

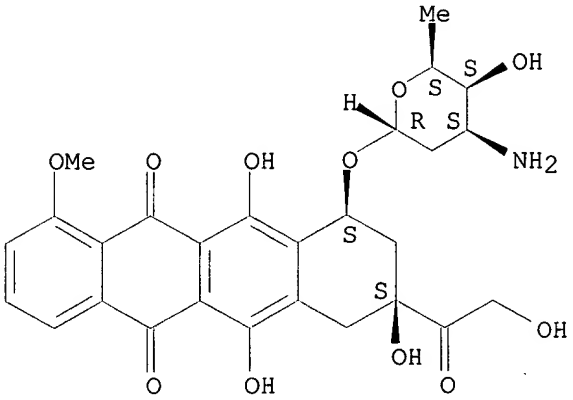
AB The invention relates to a method for assaying a DDS compd. contg. a **saccharide** compd.-modified carboxy C1-4 alkyldextran polyalc. and a drug compd. [DX8951 or doxorubicin] residue bonded to this carboxy C1-4 alkyldextran polyalc., or a DDS compd. wherein a polymer carrier is bonded to a drug compd. residue via a spacer contg. 2 to 8 amino acids bonded together via peptide bonds, which involves the step of assaying a hydrolyzate obtained by treating the DDS compd. with peptidase.

IT **23214-92-8DP**, Doxorubicin, **conjugates** with carboxy C1-4 alkyldextran polyalc. carriers **171335-80-1DP**, DX 8951, **conjugates** with carboxy C1-4 alkyldextran polyalc. carriers
RL: ANT (Analyte); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(DDS compds. and method for assaying the same)

RN 23214-92-8 HCAPLUS

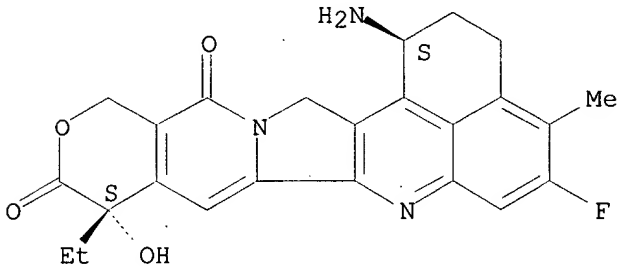
CN 5,12-Naphthacenedione, 10-[(3-amino-2,3,6-trideoxy-.alpha.-L-lyxo-hexopyranosyl)oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 171335-80-1 HCAPLUS
CN 10H,13H-Benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-10,13-dione, 1-amino-9-ethyl-5-fluoro-1,2,3,9,12,15-hexahydro-9-hydroxy-4-methyl-, (1S,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **9001-73-4**, Papain **9004-07-3**, .alpha.-Chymotrypsin
9031-96-3, Peptidase
RL: CAT (Catalyst use); USES (Uses)
(DDS compds. and method for assaying the same)
RN 9001-73-4 HCAPLUS
CN Papain (8CI, 9CI) (CA INDEX NAME)

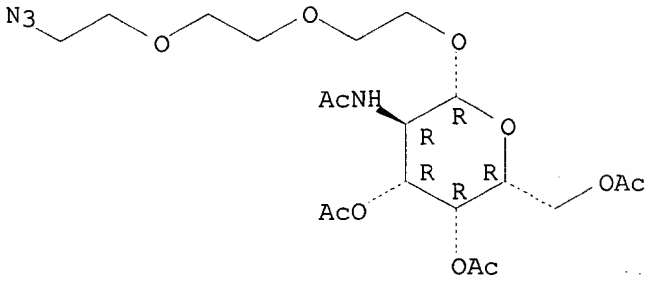
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 9004-07-3 HCAPLUS
CN Chymotrypsin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 9031-96-3 HCAPLUS
CN Peptidase (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **153253-46-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(DDS compds. and method for assaying the same)

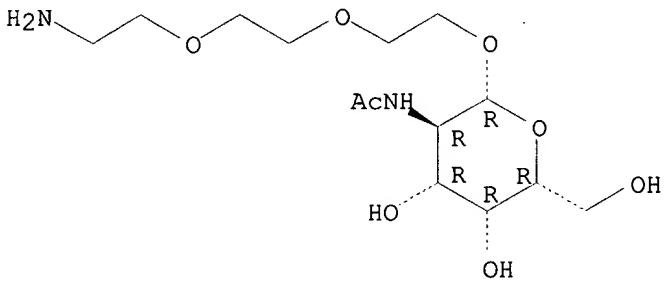
RN 153253-46-4 HCAPLUS
CN .beta.-D-Galactopyranoside, 2-[2-(2-azidoethoxy)ethoxy]ethyl 2-(acetylamino)-2-deoxy-, 3,4,6-triacetate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **267227-84-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(DDS compds. and method for assaying the same)
RN 267227-84-9 HCAPLUS
CN .beta.-D-Galactopyranoside, 2-[2-(2-aminoethoxy)ethoxy]ethyl 2-(acetylamino)-2-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **9044-05-7DP**, Carboxymethyldextran, polyalkyl and **galactose** - or N-**acetylgalactosamine**-modified, DX8951 or doxorubicin **conjugates** with **75853-32-6DP**, DX8951 or doxorubicin **conjugates** with carboxy C1-4 alkyldextran polyalc. and **200427-88-9DP**, DX8951 or doxorubicin **conjugates** with carboxy C1-4 alkyldextran polyalc. and **267227-43-0DP**, DX8951 or doxorubicin **conjugates** with carboxy C1-4 alkyldextran polyalc. and
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(DDS compds. and method for assaying the same)
RN 9044-05-7 HCAPLUS
CN Dextran, carboxymethyl ether (9CI) (CA INDEX NAME)

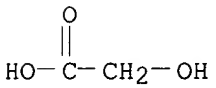
CM 1

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

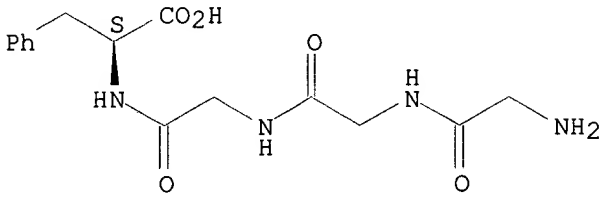
CM 2

CRN 79-14-1
CMF C2 H4 O3



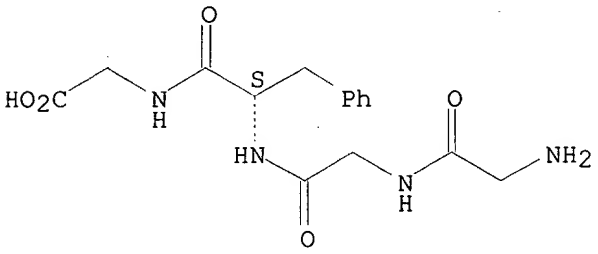
RN 75853-32-6 HCAPLUS
CN L-Phenylalanine, glycylglycylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



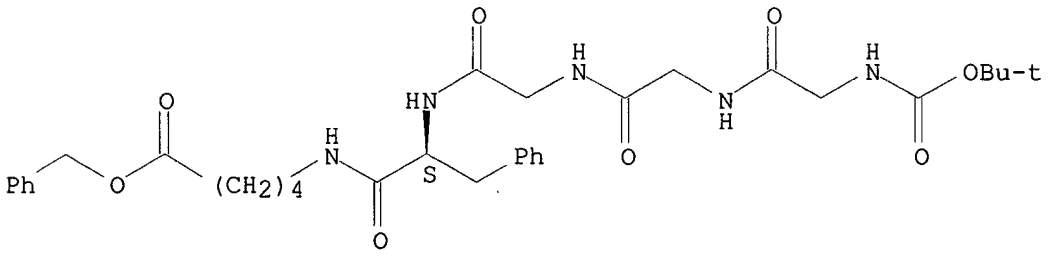
RN 200427-88-9 HCAPLUS
CN Glycine, glycylglycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 267227-43-0 HCAPLUS
CN L-Phenylalaninamide, N-[(1,1-dimethylethoxy)carbonyl]glycylglycylglycyl-N-[5-oxo-5-(phenylmethoxy)pentyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:763905 HCAPLUS
DOCUMENT NUMBER: 132:15631
TITLE: Antitumor or antiinflammatory drug composites
INVENTOR(S): **Susaki, Hiroshi; Inoue, Kazuhiro; Kuga, Hiroshi**
PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9961061	A1	19991202	WO 1999-JP2681	19990521
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9937333	A1	19991213	AU 1999-37333	19990521
EP 1080732	A1	20010307	EP 1999-919664	19990521
R: BE, CH, DE, FR, GB, IT, LI, NL, SE				
NO 2000005913	A	20010122	NO 2000-5913	20001122

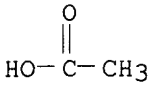
PRIORITY APPLN. INFO.: JP 1998-140915 A 19980522
WO 1999-JP2681 W 19990521

AB Drug composites useful as DDS compds., which are represented by the general formula: A-R-NH-Y-CH2-O-CO-Q (wherein A is a polymer serving as a carrier for a drug; R is a spacer comprising one amino acid mol. or one comprising 2 to 8 amino acid mols. bound to each other through peptide linkage; Y is optionally substituted phenylene; and Q is a residue of a drug compd. such as an antitumor agent). The composites permit the speedy and regioselective release of drug compds. such as antitumor or anti-inflammatory agents, thus exhibiting expected drug effects without fail. A composite of DX-8951 [(1S,9S)-1-Amino-9-ethyl-5-fluoro-2,3-dihydro-9-hydroxy-4-methyl-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-10,13(9H,15H)-dione] was prepd. from DX-8951 methanesulfonic acid salt, **dextran** polyalc. Na salt, Boc-Gly-Gly-Phe-Gly-OH, 4-aminobenzylalc., and bis(4-nitrophenyl)carbonate.

IT **64-19-7DP**, Acetic acid, reaction products with **dextran** and Dx 8951 derivs., biological studies **9004-54-0DP**, **Dextran**, polyalcs., **conjugates** with peptide-aminobenzyloxycarbonyl spacers and antitumor or antiinflammatory drugs, biological studies **9044-05-7DP**, Carboxymethyldextran, polyalcs., **conjugates** with peptide-aminobenzyloxycarbonyl spacers and antitumor or antiinflammatory drugs **171335-80-1DP**, DX 8951, reaction products with **dextran**-peptide-aminobenzyloxycarbonyl **conjugates 251459-40-2DP**, reaction products with **dextran** and acetic acid **251459-41-3DP**, reaction products with **dextran** and acetic acid
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antitumor or antiinflammatory drug **dextran** polyalc. **conjugates**)

RN 64-19-7 HCAPLUS
CN Acetic acid (7CI, 8CI, 9CI) (CA INDEX NAME)



RN 9004-54-0 HCAPLUS
CN Dextran (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 9044-05-7 HCAPLUS
CN Dextran, carboxymethyl ether (9CI) (CA INDEX NAME)

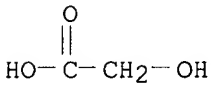
CM 1

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

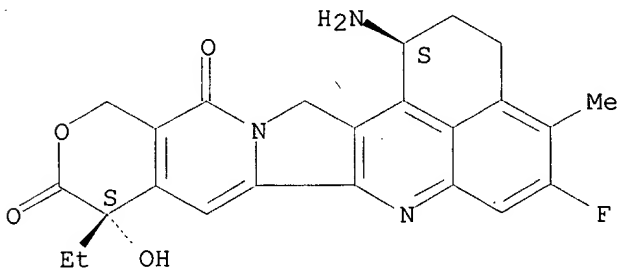
CM 2

CRN 79-14-1
CMF C2 H4 O3



RN 171335-80-1 HCAPLUS
CN 10H,13H-Benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-10,13-dione, 1-amino-9-ethyl-5-fluoro-1,2,3,9,12,15-hexahydro-9-hydroxy-4-methyl-, (1S,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

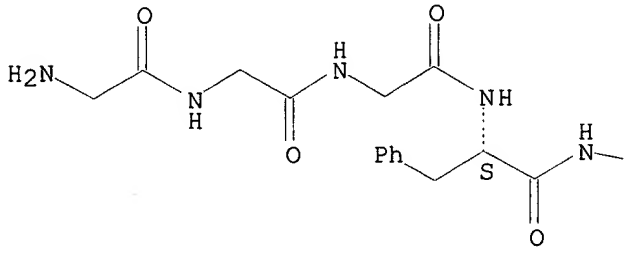


RN 251459-40-2 HCAPLUS
CN L-Phenylalaninamide, glycylglycylglycyl-N-[4-[[[[[(1S,9S)-9-ethyl-5-fluoro-

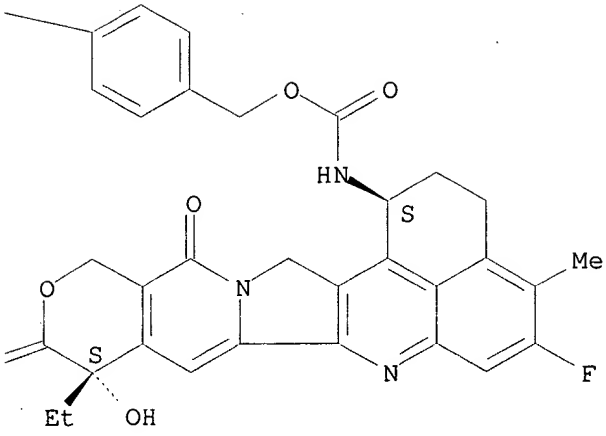
2,3,9,10,13,15-hexahydro-9-hydroxy-4-methyl-10,13-dioxo-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-1-yl]amino]carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



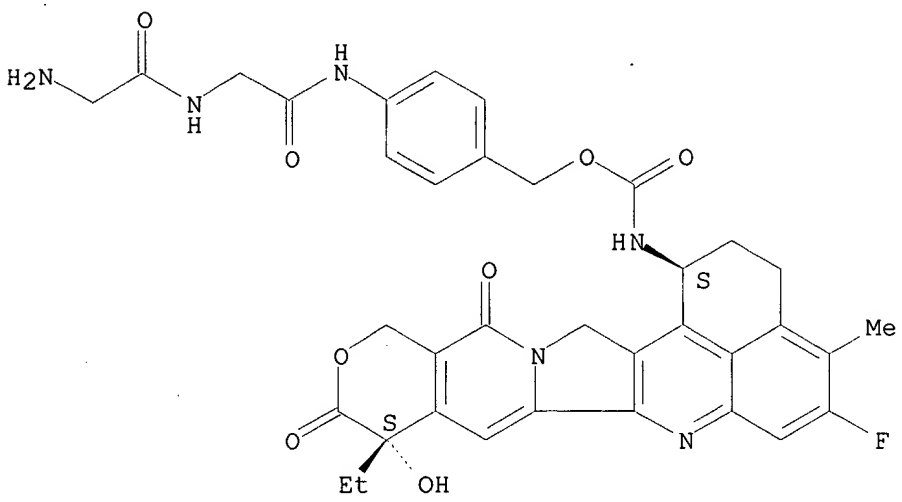
PAGE 1-B



RN 251459-41-3 HCAPLUS
CN Glycinamide, glycyl-N-[4-[[[[[(1S,9S)-9-ethyl-5-fluoro-2,3,9,10,13,15-hexahydro-9-hydroxy-4-methyl-10,13-dioxo-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-1-

yl]amino]carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

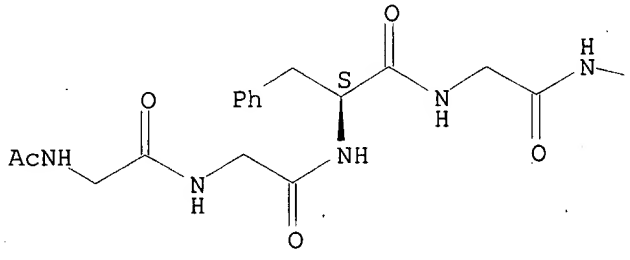
Absolute stereochemistry.

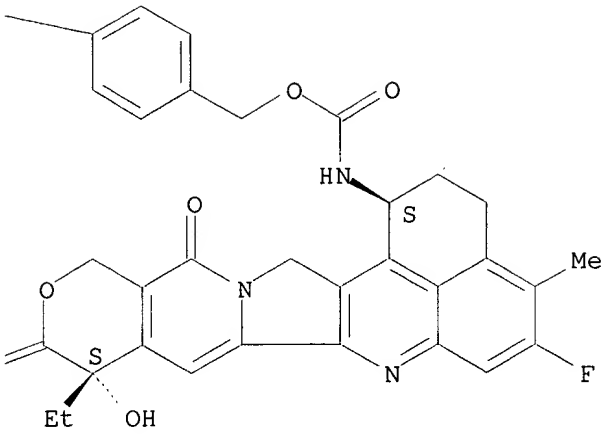


IT **251459-33-3DP**, reaction products with **dextran** and acetic acid
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of antitumor or antiinflammatory drug **dextran** polyalc. **conjugates**)
RN 251459-33-3 HCAPLUS
CN Glycinamide, N-acetylglycylglycyl-L-phenylalanyl-N-[4-[[[[[(1S,9S)-9-ethyl-5-fluoro-2,3,9,10,13,15-hexahydro-9-hydroxy-4-methyl-10,13-dioxo-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-1-yl]amino]carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

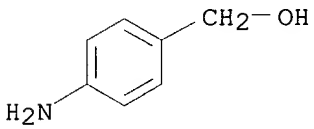
Absolute stereochemistry.

PAGE 1-A

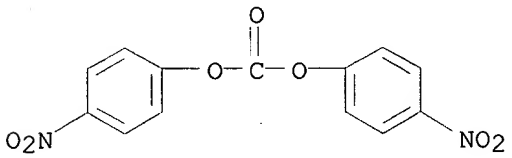




IT **623-04-1**, 4-Aminobenzylalcohol **5070-13-3**,
Bis(4-nitrophenyl)carbonate **169869-90-3 187794-49-6**
251459-34-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of antitumor or antiinflammatory drug **dextran**
polyalc. **conjugates**)
RN 623-04-1 HCAPLUS
CN Benzenemethanol, 4-amino- (9CI) (CA INDEX NAME)



RN 5070-13-3 HCAPLUS
CN Carbonic acid, bis(4-nitrophenyl) ester (9CI) (CA INDEX NAME)



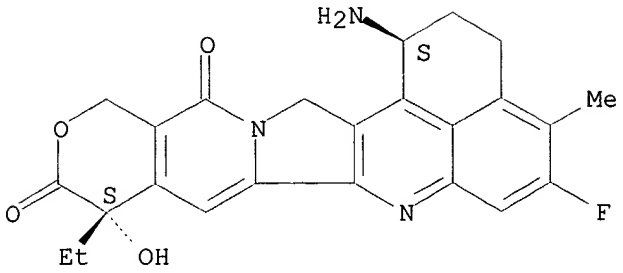
RN 169869-90-3 HCAPLUS
CN 10H,13H-Benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-10,13-dione,
1-amino-9-ethyl-5-fluoro-1,2,3,9,12,15-hexahydro-9-hydroxy-4-methyl-,
(1S,9S)-, monomethanesulfonate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 171335-80-1
CMF C24 H22 F N3 O4

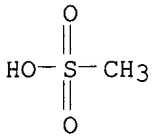
CDES *

Absolute stereochemistry.



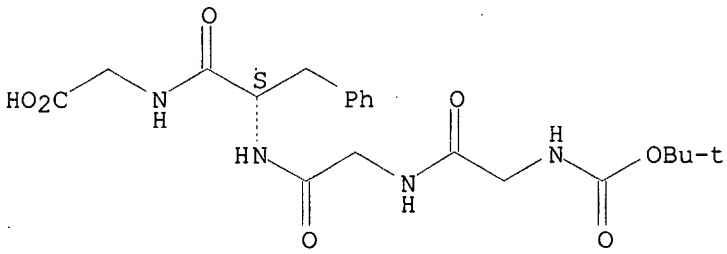
CM 2

CRN 75-75-2
CMF C H4 O3 S



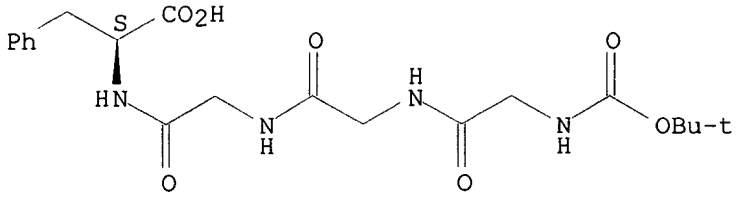
RN 187794-49-6 HCAPLUS
CN Glycine, N-[(1,1-dimethylethoxy)carbonyl]glycylglycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 251459-34-4 HCAPLUS
CN L-Phenylalanine, N-[(1,1-dimethylethoxy)carbonyl]glycylglycylglycyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **9044-05-7DP**, Carboxymethyldextran, polyalcs., Na salts
31972-52-8P 251459-28-6P 251459-29-7P
251459-31-1P 251459-32-2P 251459-35-5P
251459-36-6P 251459-37-7P 251459-38-8P
251459-39-9P 251459-40-2DP, reaction products with
dextran and acetic acid **251459-41-3P**
251459-42-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of antitumor or antiinflammatory drug **dextran** polyalc. **conjugates**)
RN 9044-05-7 HCAPLUS
CN Dextran, carboxymethyl ether (9CI) (CA INDEX NAME)

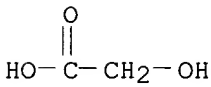
CM 1

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

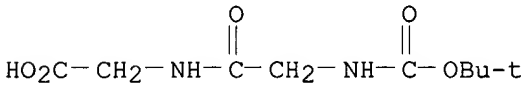
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 79-14-1
CMF C2 H4 O3

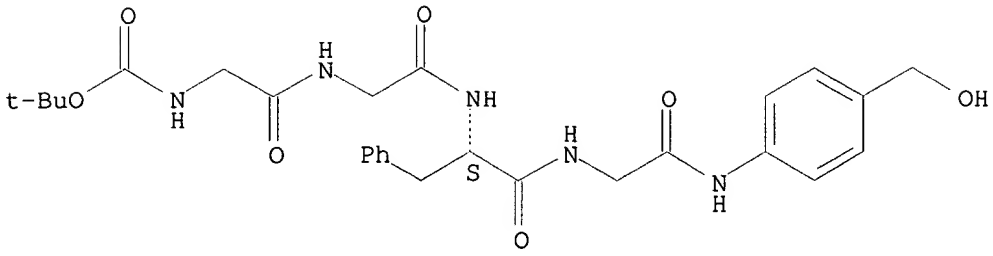


RN 31972-52-8 HCAPLUS
CN Glycine, N-[(1,1-dimethylethoxy)carbonyl]glycyl- (9CI) (CA INDEX NAME)



RN 251459-28-6 HCAPLUS
CN Glycinamide, N-[(1,1-dimethylethoxy)carbonyl]glycylglycyl-L-phenylalanyl-N-[4-(hydroxymethyl)phenyl]- (9CI) (CA INDEX NAME)

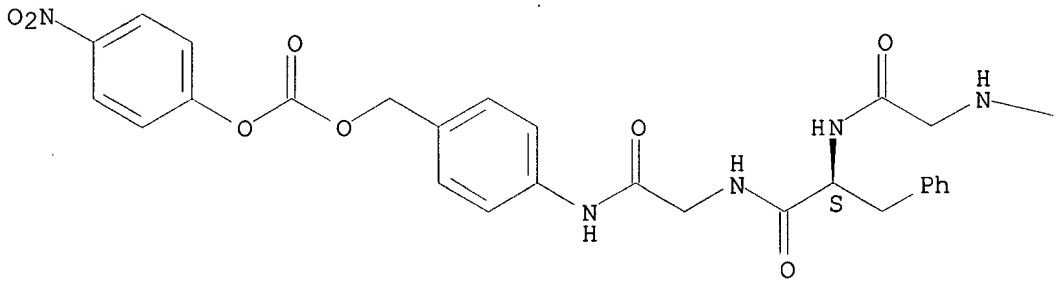
Absolute stereochemistry.



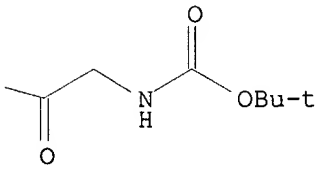
RN 251459-29-7 HCAPLUS
CN Glycinamide, N-[(1,1-dimethylethoxy)carbonyl]glycylglycyl-L-phenylalanyl-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



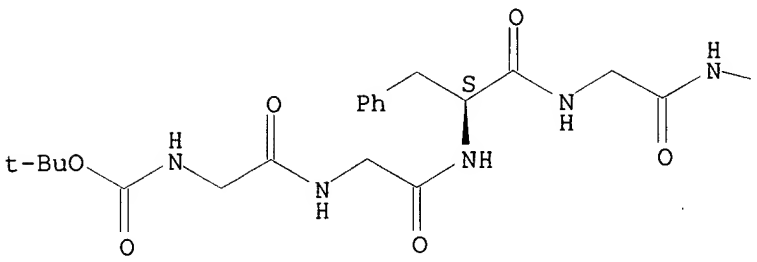
PAGE 1-B



RN 251459-31-1 HCAPLUS
CN Glycinamide, N-[(1,1-dimethylethoxy)carbonyl]glycylglycyl-L-phenylalanyl-N-[4-[[[[[(1S,9S)-9-ethyl-5-fluoro-2,3,9,10,13,15-hexahydro-9-hydroxy-4-methyl-10,13-dioxo-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-1-yl]amino]carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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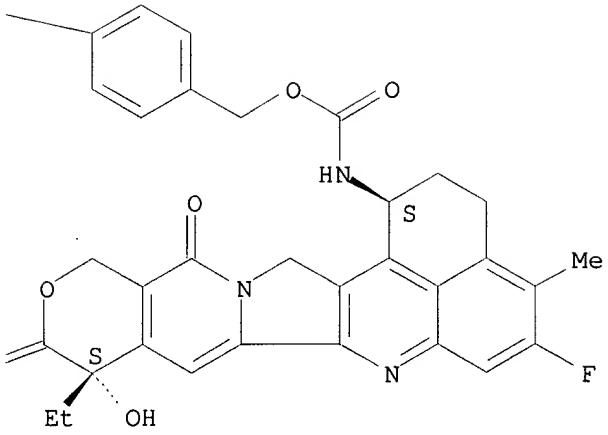
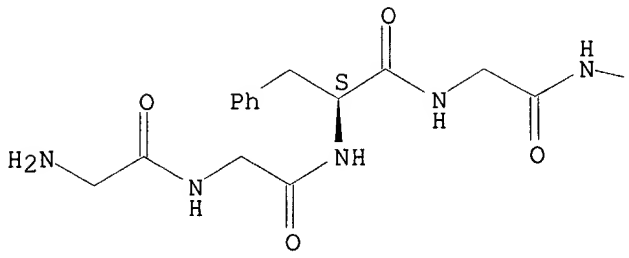


RN 251459-32-2 HCAPLUS
CN Glycinamide, glycylglycyl-L-phenylalanyl-N-[4-[[[[[(1S,9S)-9-ethyl-5-fluoro-2,3,9,10,13,15-hexahydro-9-hydroxy-4-methyl-10,13-dioxo-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-1-yl]amino]carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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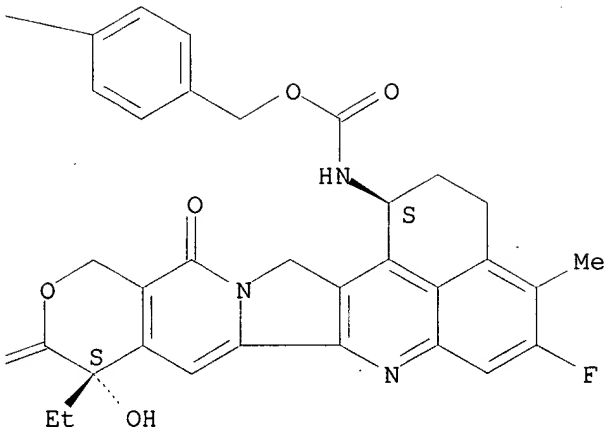

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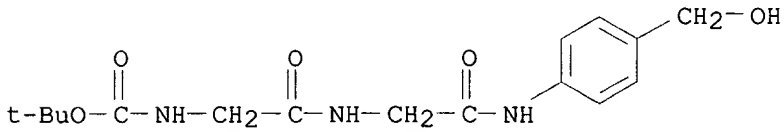
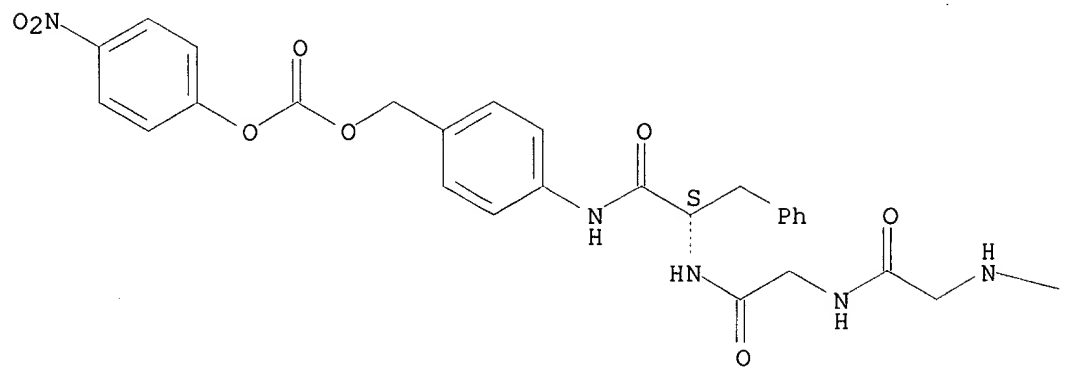
CN Glycinamide, N-[(1,1-dimethylethoxy)carbonyl]glycyl-N-[4-(hydroxymethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 251459-36-6 HCAPLUS
CN L-Phenylalaninamide, N-[(1,1-dimethylethoxy)carbonyl]glycylglycylglycyl-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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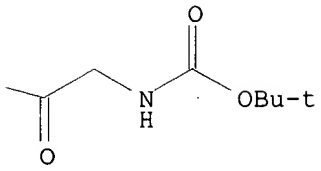
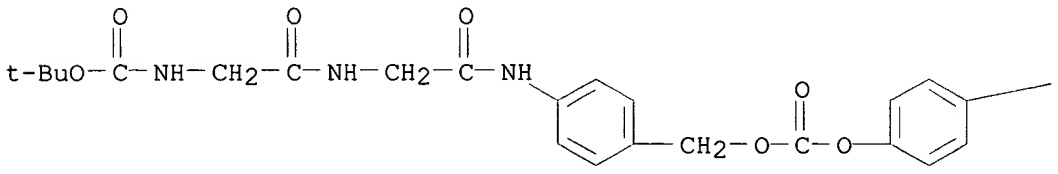


RN 251459-37-7 HCAPLUS
CN Glycinamide, N-[(1,1-dimethylethoxy)carbonyl]glycyl-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



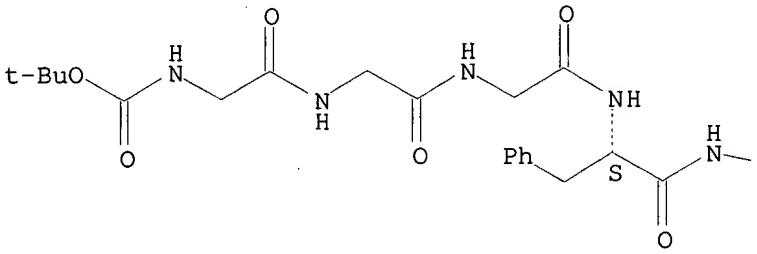
PAGE 1-B

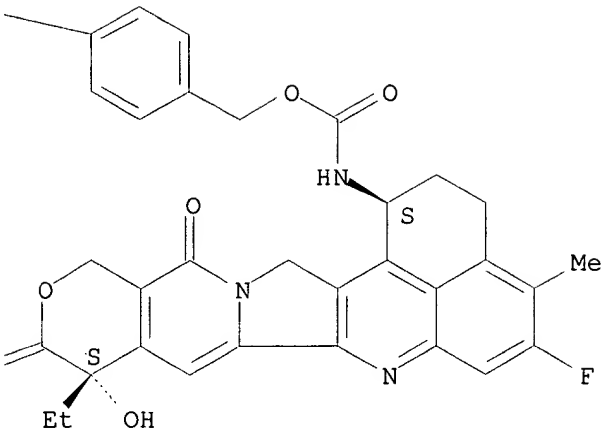
— NO_2

RN 251459-38-8 HCAPLUS
CN L-Phenylalaninamide, N-[(1,1-dimethylethoxy)carbonyl]glycylglycylglycyl-N-[4-[[[[[(1S,9S)-9-ethyl-5-fluoro-2,3,9,10,13,15-hexahydro-9-hydroxy-4-methyl-10,13-dioxo-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-1-yl]amino]carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





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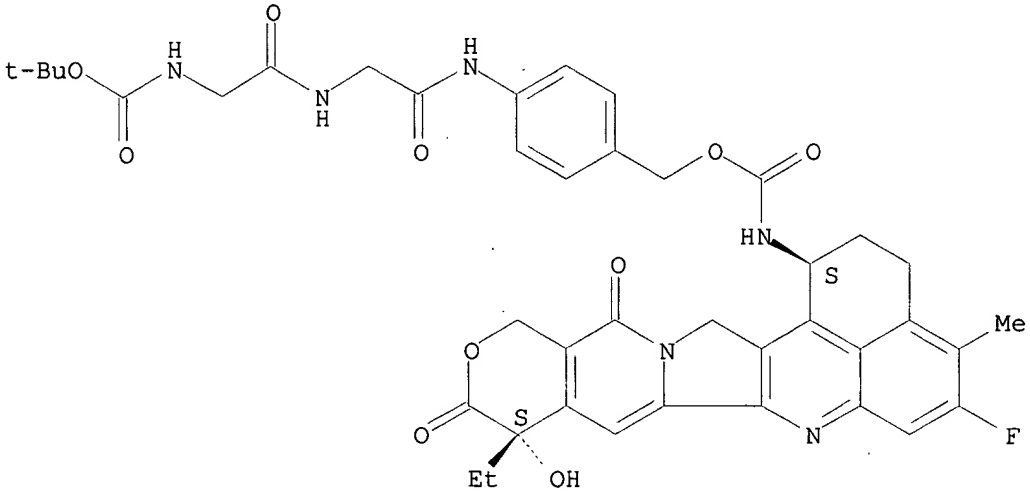
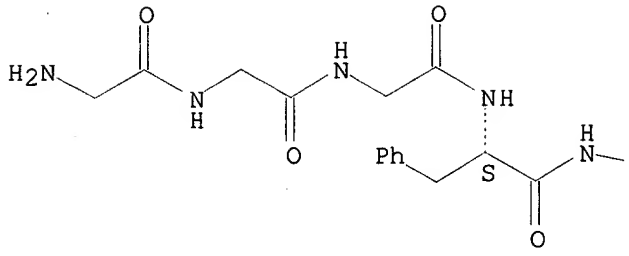
Absolute stereochemistry.



RN 251459-40-2 HCAPLUS
CN L-Phenylalaninamide, glycylglycylglycyl-N-[4-[[[[[(1S,9S)-9-ethyl-5-fluoro-2,3,9,10,13,15-hexahydro-9-hydroxy-4-methyl-10,13-dioxo-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-1-yl]amino]carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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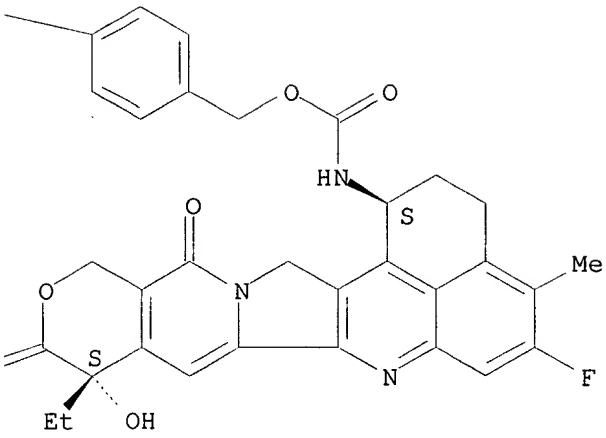
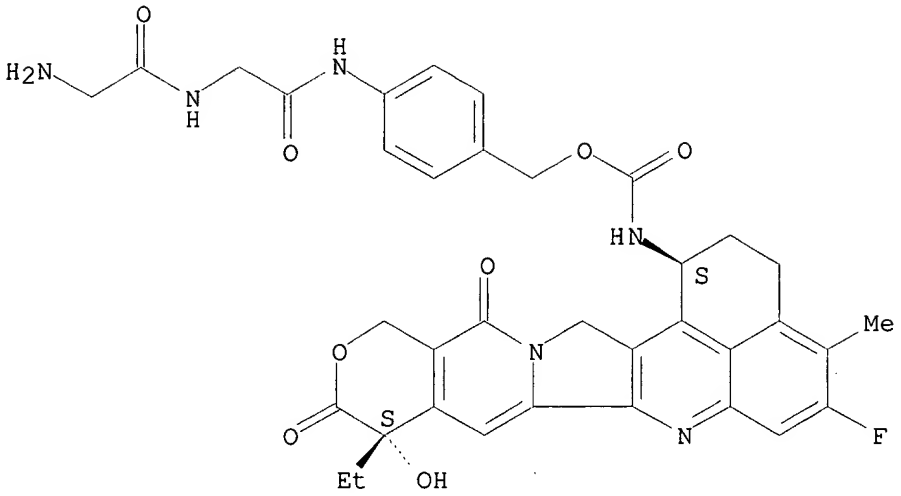


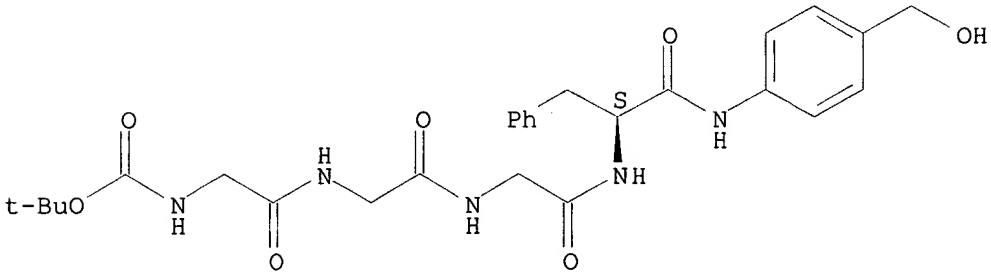
RN 251459-41-3 HCAPLUS
CN Glycinamide, glycyl-N-[4-[[[[[(1S,9S)-9-ethyl-5-fluoro-2,3,9,10,13,15-hexahydro-9-hydroxy-4-methyl-10,13-dioxo-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-1-yl]amino]carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 251459-42-4 HCAPLUS
CN L-Phenylalaninamide, N-[(1,1-dimethylethoxy)carbonyl]glycylglycylglycyl-N-[4-(hydroxymethyl)phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:1393 HCAPLUS
DOCUMENT NUMBER: 128:66510
TITLE: Process for producing drug complexes
INVENTOR(S): **Inoue, Kazuhiro; Susaki, Hiroshi; Ikeda, Masahiro**
PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan; Inoue, Kazuhiro; Susaki, Hiroshi; Ikeda, Masahiro
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9746261	A1	19971211	WO 1997-JP1915	19970605

W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

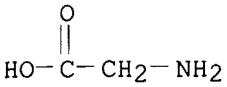
TW 409058	B	20001021	TW 1997-86107456	19970531	
AU 9729788	A1	19980105	AU 1997-29788	19970605	
AU 723442	B2	20000824			
CN 1227500	A	19990901	CN 1997-197115	19970605	
EP 955064	A1	19991110	EP 1997-924326	19970605	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI					
NO 9805667	A	19990204	NO 1998-5667	19981204	
KR 2000016371	A	20000325	KR 1998-709945	19981204	
US 6291671	B1	20010918	US 1999-147341	19990322	

PRIORITY APPLN. INFO.: JP 1996-144522 A 19960606
WO 1997-JP1915 W 19970605

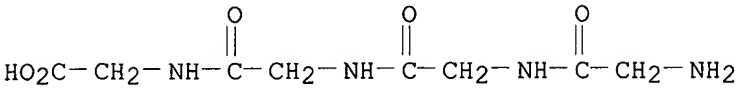
AB The invention relates to a process for producing drug complexes wherein a carboxylated **polysaccharide** deriv. is bonded to a medicinal compd. residue via a spacer consisting of an amino acid or a spacer consisting of two to eight amino acids bonded to each other via peptide bonds, or drug complexes wherein a carboxylated **polysaccharide** deriv. is bonded to a medicinal compd. residue via no spacer, which is characterized by reacting in a nonaq. system an org. amine salt of the carboxylated **polysaccharide** deriv. with the medicinal compd. or the spacer bonded thereto. Thus, the reaction between the carboxylated **polysaccharide** deriv. and the medicinal compd. bonded to the spacer, etc., can be effected to achieve a high yield and side reactions can be inhibited in the case where, for example, the medicinal compd. is one having a lactone ring.

IT **56-40-6DP**, Glycine, **conjugates** with antitumor and antiinflammatory drugs and polysaccharides, biological studies **637-84-3DP**, **conjugates** with antitumor and antiinflammatory drugs and polysaccharides **721-90-4DP**, **conjugates** with antitumor and antiinflammatory drugs and polysaccharides **9004-54-0DP**, **Dextran**, oxidn. and redn. derivs., **conjugates** with antitumor and antiinflammatory drugs and peptide spacers, biological studies **14656-09-8DP**, **conjugates** with antitumor and antiinflammatory drugs and polysaccharides **23214-92-8DP**, Doxorubicin, **conjugates** with peptide spacers and polysaccharides **66328-74-3DP**, **conjugates** with antitumor and antiinflammatory drugs and polysaccharides **143655-66-7DP**, **conjugates** with peptide spacers and polysaccharides **171335-80-1DP**, **conjugates** with peptide spacers and polysaccharides **184585-36-2DP**, **conjugates** with antitumor and antiinflammatory drugs and polysaccharides **200427-88-9DP**, **conjugates** with antitumor and antiinflammatory drugs and polysaccharides **200427-89-0DP**, **conjugates** with antitumor and antiinflammatory drugs and polysaccharides **200428-32-6DP**, **conjugates** with peptide spacers and polysaccharides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(anticancer and antiinflammatory drug-**polysaccharide** **conjugates**)

RN 56-40-6 HCAPLUS
CN Glycine (8CI, 9CI) (CA INDEX NAME)

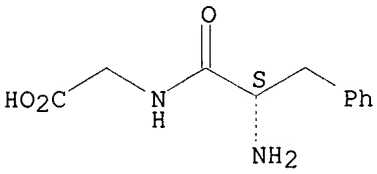


RN 637-84-3 HCAPLUS
CN Glycine, glycylglycylglycyl- (9CI) (CA INDEX NAME)



RN 721-90-4 HCAPLUS
CN Glycine, L-phenylalanyl- (9CI) (CA INDEX NAME)

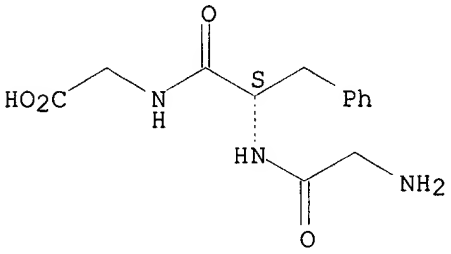
Absolute stereochemistry.



RN 9004-54-0 HCAPLUS
CN Dextran (9CI) (CA INDEX NAME)

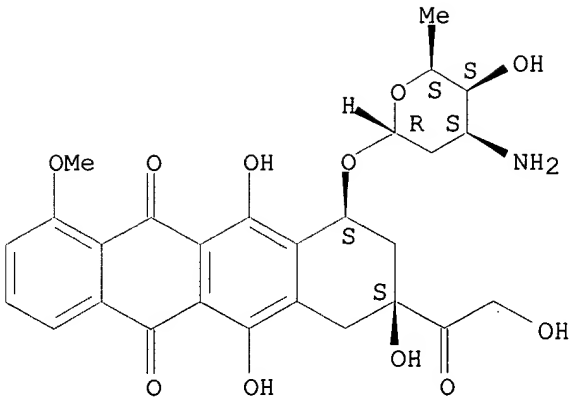
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 14656-09-8 HCAPLUS
CN Glycine, glycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



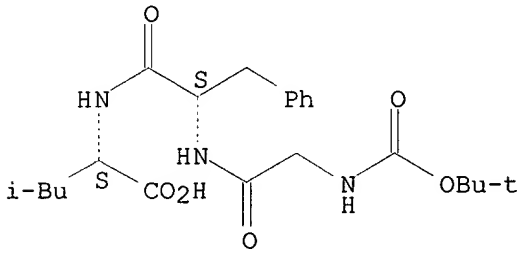
RN 23214-92-8 HCAPLUS
CN 5,12-Naphthacenedione, 10-[(3-amino-2,3,6-trideoxy-.alpha.-L-lyxo-hexopyranosyl)oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



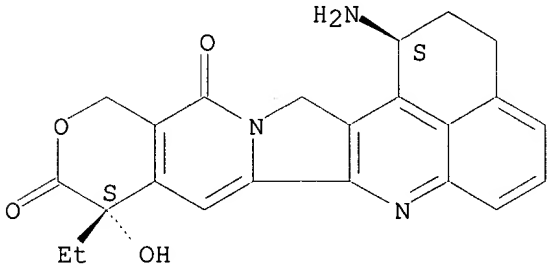
RN 66328-74-3 HCAPLUS
CN L-Leucine, N-[(1,1-dimethylethoxy)carbonyl]glycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



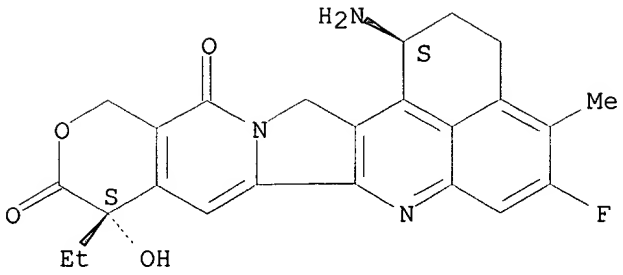
RN 143655-66-7 HCAPLUS
CN 10H,13H-Benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-10,13-dione, 1-amino-9-ethyl-1,2,3,9,12,15-hexahydro-9-hydroxy-, (1S-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



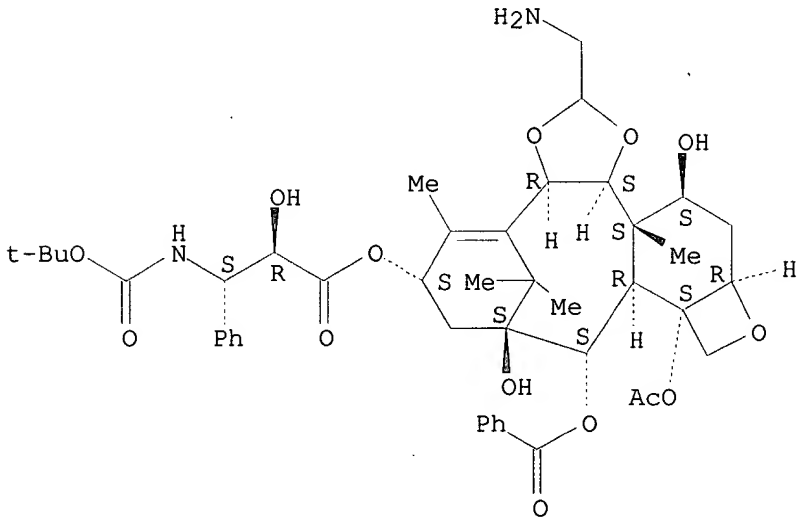
RN 171335-80-1 HCAPLUS
CN 10H,13H-Benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-10,13-dione, 1-amino-9-ethyl-5-fluoro-1,2,3,9,12,15-hexahydro-9-hydroxy-4-methyl-, (1S,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



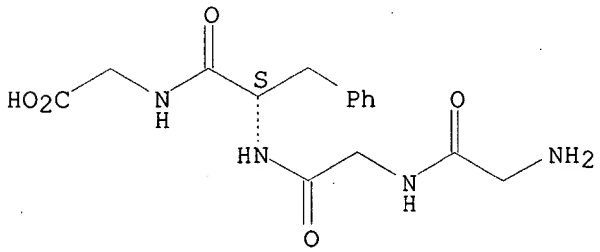
RN 184585-36-2 HCAPLUS
CN Benzenepropanoic acid, .beta.-[[(1,1-dimethylethoxy)carbonyl]amino]-.alpha.-hydroxy-, 2a-(acetyloxy)-10-(aminomethyl)-3-(benzoyloxy)-2a,2b,3,4,5,6,8a,11a,11b,12,13,13a-dodecahydro-4,12-dihydroxy-7,11b,14,14-tetramethyl-4,8-methano-2H-oxeto[3'',2'':3',4']benzo[1',2':3,4]cyclodeca[1,2-d][1,3]dioxol-6-yl ester, [2aS,2bR,3S,4S,6S(.alpha.R,.beta.S),8aR,11aS,11bS,12S,13aR]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 200427-88-9 HCAPLUS
CN Glycine, glycylglycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

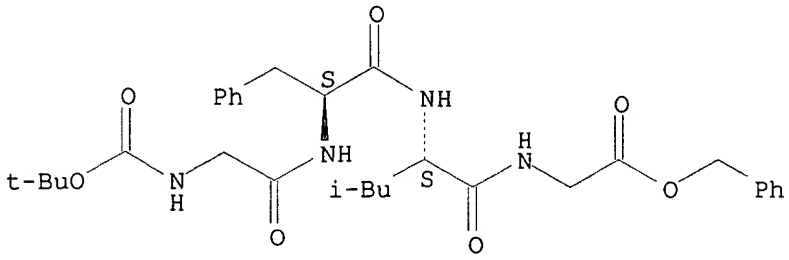
Absolute stereochemistry.



RN 200427-89-0 HCAPLUS

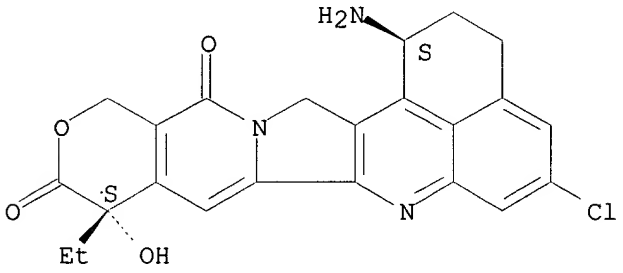
CN Glycine, N-[(1,1-dimethylethoxy)carbonyl]glycyl-L-phenylalanyl-L-leucyl-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 200428-32-6 HCAPLUS
CN 10H,13H-Benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-10,13-dione, 1-amino-5-chloro-9-ethyl-1,2,3,9,12,15-hexahydro-9-hydroxy-, (1S-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L13 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:1392 HCAPLUS
DOCUMENT NUMBER: 128:66509
TITLE: Drug complexes
INVENTOR(S): **Inoue, Kazuhiro; Susaki, Hiroshi; Ikeda, Masahiro; Kuga, Hiroshi;** Kumazawa, Eiji; Togo, Akiko
PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan; Drug Delivery System Institute, Ltd.; Inoue, Kazuhiro; Susaki, Hiroshi; Ikeda, Masahiro; Kuga, Hiroshi; Kumazawa, Eiji; Togo, Akiko
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9746260	A1	19971211	WO 1997-JP1914	19970605

W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU,

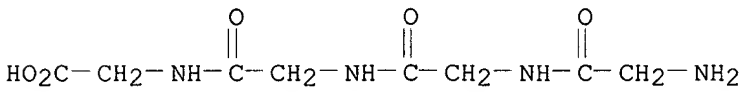
TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9729787	A1	19980105	AU 1997-29787	19970605	
AU 723392	B2	20000824			
EP 916348	A1	19990519	EP 1997-924325	19970605	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI					
CN 1227499	A	19990901	CN 1997-197008	19970605	
NO 9805666	A	19990204	NO 1998-5666	19981204	
KR 2000016558	A	20000325	KR 1998-710148	19981207	
PRIORITY APPLN. INFO.:			JP 1996-144421	A 19960606	
			WO 1997-JP1914	W 19970605	

AB The invention relates to drug complexes wherein a carboxy (C1-4)alkyldextran polyalc., which has been treated under such conditions as to allow the substantially complete formation of the polyalc., is bonded to the residue of a medicinal compd. such as an antitumor agent [e.g. doxorubicin] via a spacer consisting of one amino acid or a spacer consisting of two to eight amino acids bonded to each other via peptide bonds. The complexes are excellent in the tumor site selectivity and thus can exhibit a high antitumor effect with relieved expression of toxicity.

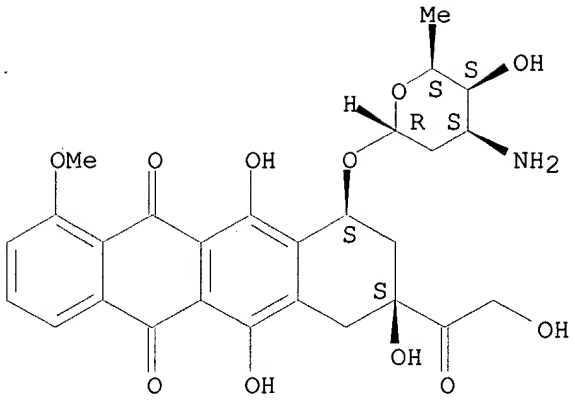
IT **637-84-3D, conjugates** with antitumor or antiinflammatory drugs and carboxyalkyldextran polyalcs. **23214-92-8D,** Doxorubicin, **conjugates** with peptide spacer and carboxyalkyldextran polyalcs. **143655-66-7D,** DW 8089, **conjugates** with peptide spacers and carboxyalkyldextran polyalcs. **171335-80-1D, conjugates** with peptide spacer and carboxyalkyldextran polyalcs. **184585-36-2D,** D 51-7059, **conjugates** with peptide spacers and carboxyalkyldextran polyalcs. **200427-88-9D, conjugates** with antitumor or antiinflammatory drugs and carboxyalkyldextran polyalcs. **200438-24-0D,** DW 8286, **conjugates** with peptide spacers and carboxyalkyldextran polyalcs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor or antiinflammatory drug **dextran** polyalc. **conjugates**)

RN 637-84-3 HCAPLUS
CN Glycine, glycylglycylglycyl- (9CI) (CA INDEX NAME)



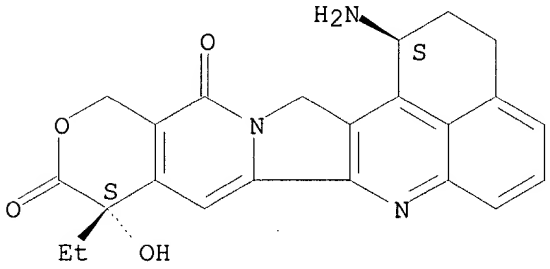
RN 23214-92-8 HCAPLUS
CN 5,12-Naphthacenedione, 10-[(3-amino-2,3,6-trideoxy-.alpha.-L-lyxo-hexopyranosyl)oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-, (8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



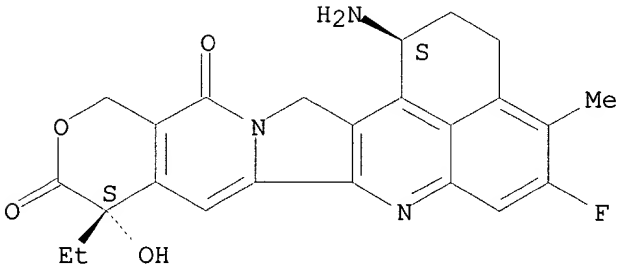
RN 143655-66-7 HCAPLUS
CN 10H,13H-Benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-10,13-dione, 1-amino-9-ethyl-1,2,3,9,12,15-hexahydro-9-hydroxy-, (1S-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 171335-80-1 HCAPLUS
CN 10H,13H-Benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-10,13-dione, 1-amino-9-ethyl-5-fluoro-1,2,3,9,12,15-hexahydro-9-hydroxy-4-methyl-, (1S,9S)- (9CI) (CA INDEX NAME)

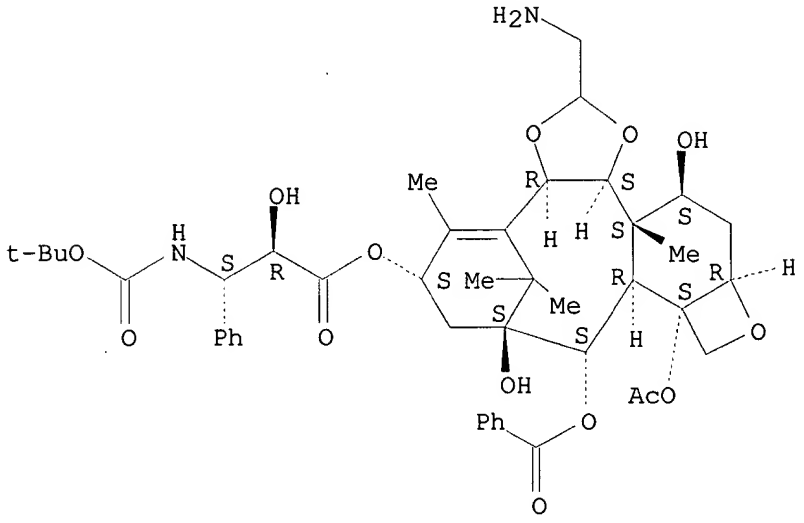
Absolute stereochemistry.



RN 184585-36-2 HCAPLUS
CN Benzenepropanoic acid, .beta.-[[(1,1-dimethylethoxy)carbonyl]amino]-.alpha.-hydroxy-, 2a-(acetyloxy)-10-(aminomethyl)-3-(benzoyloxy)-2a,2b,3,4,5,6,8a,11a,11b,12,13,13a-dodecahydro-4,12-dihydroxy-7,11b,14,14-tetramethyl-4,8-methano-2H-oxeto[3'',2'':3',4']benzo[1',2':3,4]cyclodeca[1

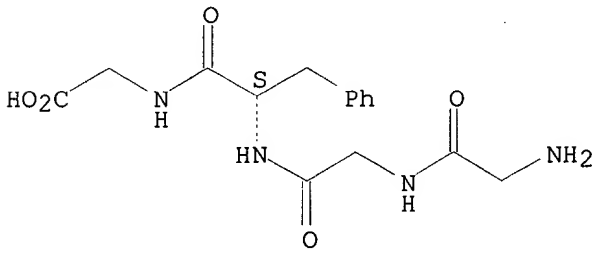
,2-d][1,3]dioxol-6-yl ester, [2aS,2bR,3S,4S,6S(.alpha.R,.beta.S),8aR,11aS, 11bS,12S,13aR]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



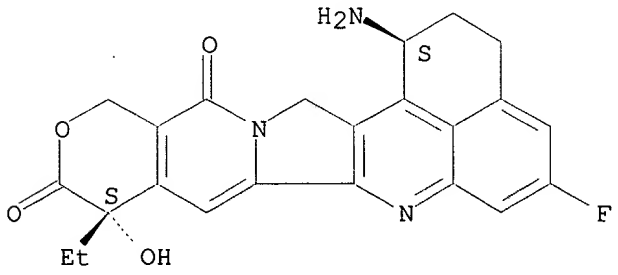
RN 200427-88-9 HCAPLUS
CN Glycine, glycylglycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



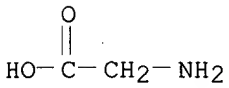
RN 200438-24-0 HCAPLUS
CN 10H,13H-Benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-10,13-dione, 1-amino-9-ethyl-5-fluoro-1,2,3,9,12,15-hexahydro-9-hydroxy-, (1S-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



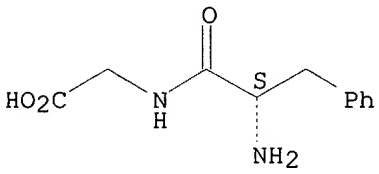
IT **56-40-6DP**, Glycine, **conjugates** with antitumor or antiinflammatory drugs and carboxyalkyldextran polyalcs., preparation **721-90-4DP**, **conjugates** with antitumor or antiinflammatory drugs and carboxyalkyldextran polyalcs. **9004-54-0DP**, **Dextran**, oxidn. and redn. derivs., **conjugates** with peptide spacers and antitumor or antiinflammatory drugs and carboxyalkyldextran polyalcs., preparation **14656-09-8DP**, **conjugates** with antitumor or antiinflammatory drugs and carboxyalkyldextran polyalcs. **66328-74-3P 200427-89-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(antitumor or antiinflammatory drug **dextran** polyalc. **conjugates**)

RN 56-40-6 HCAPLUS
CN Glycine (8CI, 9CI) (CA INDEX NAME)



RN 721-90-4 HCAPLUS
CN Glycine, L-phenylalanyl- (9CI) (CA INDEX NAME)

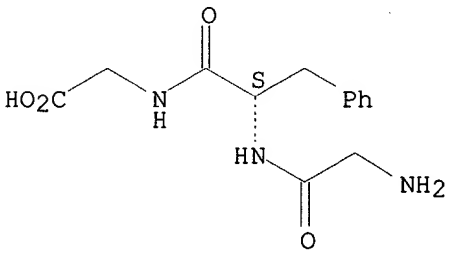
Absolute stereochemistry.



RN 9004-54-0 HCAPLUS
CN Dextran (9CI) (CA INDEX NAME)

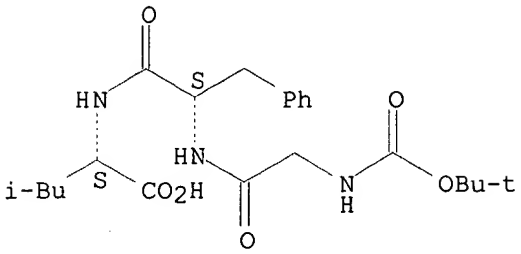
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 14656-09-8 HCAPLUS
CN Glycine, glycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



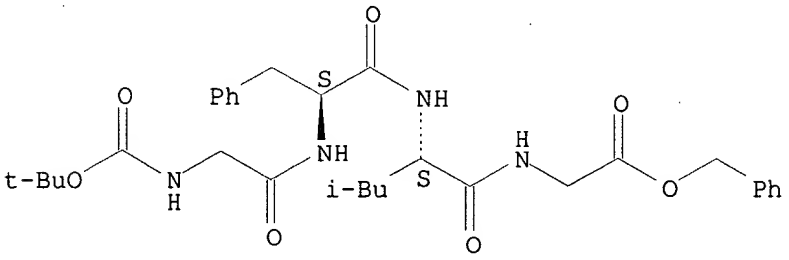
RN 66328-74-3 HCAPLUS
CN L-Leucine, N-[(1,1-dimethylethoxy)carbonyl]glycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 200427-89-0 HCAPLUS
CN Glycine, N-[(1,1-dimethylethoxy)carbonyl]glycyl-L-phenylalanyl-L-leucyl-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



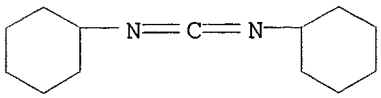
L13 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:307289 HCAPLUS
DOCUMENT NUMBER: 120:307289
TITLE: Tissue-targeting ability of **saccharide** -poly(L-lysine) **conjugates**
AUTHOR(S): Gonsho, Akinori; Irie, Kunihiko; **Susaki, Hiroshi**; Iwasawa, Hiroyuki; Okuno, Satoshi; Sugawara, Tamio
CORPORATE SOURCE: Drug Delivery Syst. Inst., Ltd., Sci. Univ. Tokyo, Noda, 278, Japan
SOURCE: Biol. Pharm. Bull. (1994), 17(2), 275-82
CODEN: BPBLEO; ISSN: 0918-6158
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To evaluate the effect of introducing a **saccharide** moiety to poly(amino acids) on tissue distribution, several glycoconjugates of .epsilon.-(2-methoxyethoxyacetyl)-poly(L-lysine) of three mol. wts. were synthesized using an octylene spacer between the sugar and polymer chain. Methoxyethoxyacetylation of the .epsilon.-amino group of the lysine unit in poly(L-lysine) was useful for avoiding nonspecific distribution to many tissues as the result of cationic charges. The tissue-targeting ability of each **saccharide** moiety was considered as the actual amt. changed in each tissue caused by **saccharide** modification. **Galactose** terminated saccharides such as **galactose**, lactose and N-**acetylgalactosamine** accumulated exclusively in the liver, probably by the hepatic receptor. These **conjugates** could therefore be good carriers for a drug delivery system to the liver. On the other hand, the mannosyl and fucosyl **conjugates** were preferentially delivered to the reticuloendothelial systems such as those

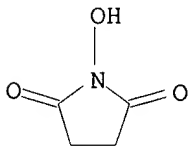
in the liver, spleen and bone marrow. In particular, fucosyl **conjugates** accumulated more in the bone marrow than in the spleen. Xylosyl **conjugates** accumulated mostly in the liver and lung. Generally, the accumulated amt. in the target tissue increased with increasing mol. wt. and an increased no. of saccharides on one mol. of polymer.

IT **538-75-0**, 1,3-Dicyclohexylcarbodiimide **6066-82-6**, N-Hydroxysuccinimide **16024-56-9**, 2-Methoxyethoxyacetic acid **25988-63-0**, Poly(L-lysine) hydrobromide **34071-95-9** **64186-24-9** **65567-26-2**, 8-Hydrazinocarbonyloctyl .beta.-D-galactopyranoside
RL: BIOL (Biological study)
(in prepn. of **saccharide**-poly(L-lysine) **conjugate**)

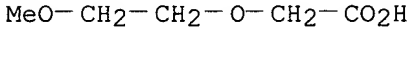
RN 538-75-0 HCAPLUS
CN Cyclohexanamine, N,N'-methanetetraylbis- (9CI) (CA INDEX NAME)



RN 6066-82-6 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-hydroxy- (9CI) (CA INDEX NAME)



RN 16024-56-9 HCAPLUS
CN Acetic acid, (2-methoxyethoxy)- (8CI, 9CI) (CA INDEX NAME)



RN 25988-63-0 HCAPLUS
CN L-Lysine, homopolymer, hydrobromide (9CI) (CA INDEX NAME)

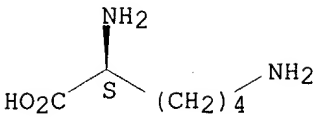
CM 1

CRN 25104-18-1
CMF (C6 H14 N2 O2)x
CCI PMS

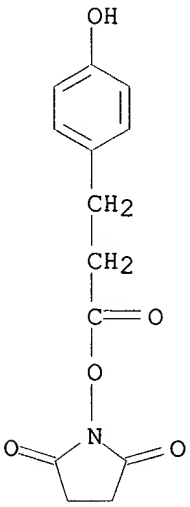
CM 2

CRN 56-87-1
CMF C6 H14 N2 O2
CDES 5:L

Absolute stereochemistry.

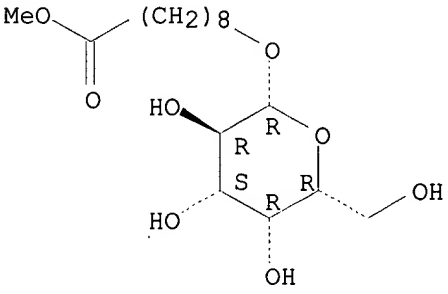


RN 34071-95-9 HCAPLUS
CN 2,5-Pyrrolidinedione, 1-[3-(4-hydroxyphenyl)-1-oxopropoxy]- (9CI) (CA INDEX NAME)



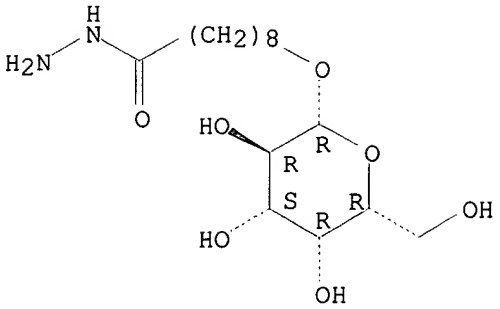
RN 64186-24-9 HCAPLUS
CN Nonanoic acid, 9-(.beta.-D-galactopyranosyloxy)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

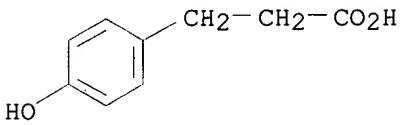


RN 65567-26-2 HCAPLUS
CN Nonanoic acid, 9-(.beta.-D-galactopyranosyloxy)-, hydrazide (9CI) (CA INDEX NAME)

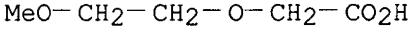
Absolute stereochemistry.



IT **501-97-3DP**, 3-(4-Hydroxyphenyl)propanoic acid, reaction products with polylysine **16024-56-9DP**, reaction products with polylysine **83345-63-5DP**, reaction products with polylysine and hydroxyphenylpropanoic acid derivs.
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and tissue-targeting ability of)
RN 501-97-3 HCAPLUS
CN Benzenepropanoic acid, 4-hydroxy- (9CI) (CA INDEX NAME)

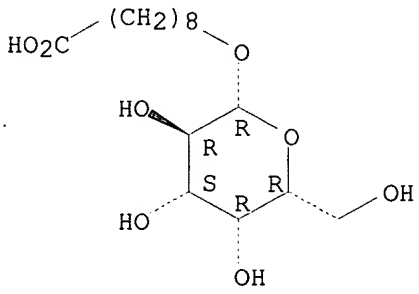


RN 16024-56-9 HCAPLUS
CN Acetic acid, (2-methoxyethoxy)- (8CI, 9CI) (CA INDEX NAME)



RN 83345-63-5 HCAPLUS
CN Nonanoic acid, 9-(.beta.-D-galactopyranosyloxy)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L13 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:428456 HCAPLUS
DOCUMENT NUMBER: 119:28456
TITLE: Synthesis of 8-aminooctyl glycopyranosides and of their **conjugates** with poly(L-glutamic acid)

having a 2-(4-hydroxyphenyl)ethylamino group for radiolabeling

AUTHOR(S): Sugawara, Tamio; **Susaki, Hiroshi**; Nogusa, Hideo; Gonsho, Akinori; Iwasawa, Hiroyuki; Irie, Kunihiko; Ito, Yukio; Shibukawa, Mitsuru

CORPORATE SOURCE: Drug Deliver Syst. Inst. Ltd., Noda, 278, Japan

SOURCE: Carbohydr. Res. (1993), 238, 163-84
CODEN: CRBRAT; ISSN: 0008-6215

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 8-Aminooctyl glycopyranosides of .beta.-D-**galactose**, .beta.-L-frucose, .alpha.- and .beta.-D-xyloses, .alpha.- and .beta.-D-mannoses, 2-acetamido-2-deoxy-.beta.-D-mannose, and 2-acetamido-2-deoxy-.alpha.-L-fucose were synthesized under Koenigs-Knorr type glycosylation reaction conditions using the corresponding glycopyranosyl halides or 2-azido-2-deoxy-glycopyranosyl halides and N-(8-hydroxyoctyl)phthalimide. Condensation of 8-aminooctyl glycopyranosides of .beta.-D-**galactose**, .beta.-L-fucose, .alpha.-D-xylose, and .alpha.- and .beta.-D-mannoses with poly(L-glutamic acid) in the presence of 4-(2-aminoethyl)phenol and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride or 2-ethoxy-1-ethoxycarbonyl-1,2-dihydroquinoline as a condensation reagent, gave [8-(.beta.-D-galactopyranosyloxy)octylamine]36-[2-(4-hydroxyphenyl)ethylamine]3-poly(L-glutamic acid) **conjugate**, [8-(.beta.-L-fucopyranosyloxy)octylamine]16-[2-(4-hydroxyphenyl)ethylamine]4-poly(L-glutamic acid) **conjugate**, [8-(.alpha.-D-xylopyranosyloxy)octylamine]12-[2-(4-hydroxyphenyl)ethylamine]2-poly(L-glutamic acid) **conjugate**, [8-(.alpha.-D-mannopyranosyloxy)octylamine]18-[2-(4-hydroxyphenyl)ethylamine]5-poly(L-glutamic acid) **conjugate**, and [8-(.beta.-D-mannopyranosyloxy)octylamine]27-[2-(4-hydroxyphenyl)ethylamine]2-poly(L-glutamic acid) **conjugate**, resp. The plasma elimination rates of [125I]-labeled carbohydrate-poly(L-glutamic acid) **conjugates** bearing 8-(.beta.-D-galactopyranosyloxy)octylamino and 8-(.alpha.-D-mannopyransoyloxy)octylamino residues after i.v. administration to rats were more rapid than that of [125I]-labeled [2-(4-hydroxyphenyl)ethylamine]5-poly(L-glutamic acid) **conjugate**.

IT **26247-79-0**, Poly(L-glutamic acid) sodium salt **28680-04-8**
RL: RCT (Reactant)
(acid hydrolysis of)

RN 26247-79-0 HCAPLUS

CN L-Glutamic acid, homopolymer, sodium salt (9CI) (CA INDEX NAME)

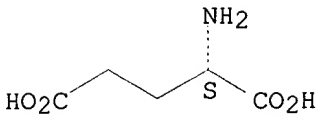
CM 1

CRN 25513-46-6
CMF (C5 H9 N O4)x
CCI PMS

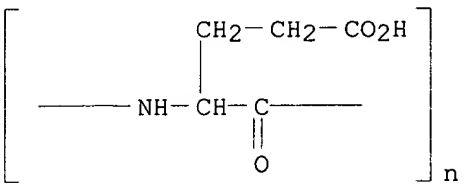
CM 2

CRN 56-86-0
CMF C5 H9 N O4
CDES 5:L

Absolute stereochemistry.

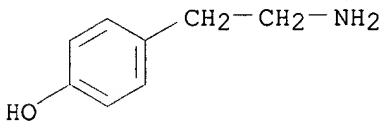


RN 28680-04-8 HCAPLUS
CN Poly[imino[(1S)-1-(2-carboxyethyl)-2-oxo-1,2-ethanediyl]], sodium salt (9CI) (CA INDEX NAME)



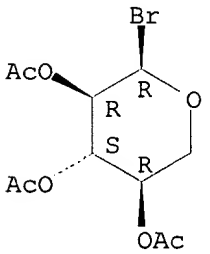
●x Na

IT **51-67-2**, 4-(2-Aminoethyl)phenol
RL: RCT (Reactant)
(amidation by, of polyglutamic acid)
RN 51-67-2 HCAPLUS
CN Phenol, 4-(2-aminoethyl)- (9CI) (CA INDEX NAME)



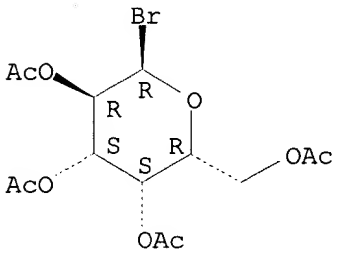
IT **3068-31-3 3068-32-4 16741-27-8**
65827-59-0 92470-93-4, 2,3,4,6-Tetra-O-benzyl-.alpha.-D-mannopyranosyl chloride **95451-93-7**, 3,4,6-Tri-O-acetyl-2-azido-2-deoxy-.alpha.-D-mannopyranosyl bromide **143528-49-8**
RL: RCT (Reactant)
(glycosidation by, of (hydroxyoctyl)phthalimide)
RN 3068-31-3 HCAPLUS
CN .alpha.-D-Xylopyranosyl bromide, triacetate (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



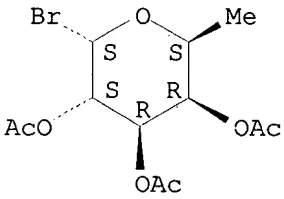
RN 3068-32-4 HCAPLUS
CN .alpha.-D-Galactopyranosyl bromide, tetraacetate (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



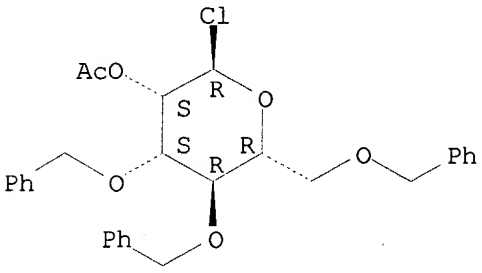
RN 16741-27-8 HCAPLUS
CN .alpha.-L-Galactopyranosyl bromide, 6-deoxy-, triacetate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



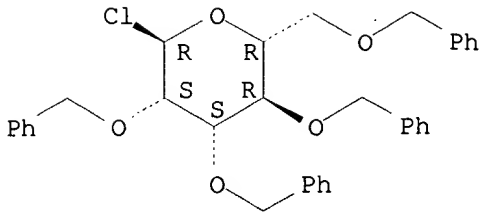
RN 65827-59-0 HCAPLUS
CN .alpha.-D-Mannopyranosyl chloride, 3,4,6-tris-O-(phenylmethyl)-, acetate (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



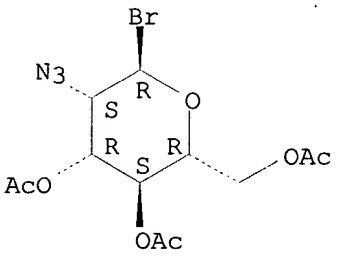
RN 92470-93-4 HCAPLUS
CN .alpha.-D-Mannopyranosyl chloride, 2,3,4,6-tetrakis-O-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



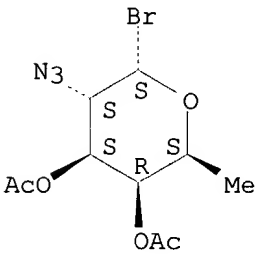
RN 95451-93-7 HCAPLUS
CN .alpha.-D-Mannopyranosyl bromide, 2-azido-2-deoxy-, 3,4,6-triacetate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

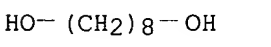


RN 143528-49-8 HCAPLUS
CN .alpha.-L-Galactopyranosyl bromide, 2-azido-2,6-dideoxy-, 3,4-diacetate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

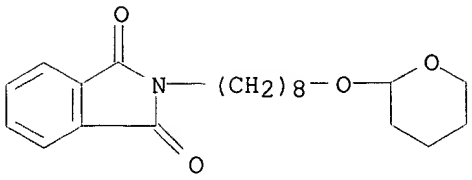


IT **629-41-4**, 1,8-Octanediol
RL: RCT (Reactant)
(partial tetrahydropyranylation of)
RN 629-41-4 HCAPLUS
CN 1,8-Octanediol (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

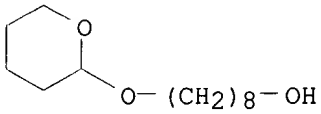


IT **148180-09-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and acid-catalyzed hydrolysis of)
RN 148180-09-0 HCAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[8-[(tetrahydro-2H-pyran-2-yl)oxy]octyl]-

(9CI) (CA INDEX NAME)

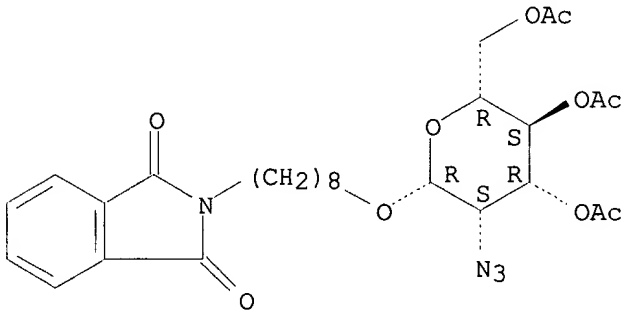


IT **51326-52-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and amidation of, with phthalimide)
RN 51326-52-4 HCAPLUS
CN 1-Octanol, 8-[(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)



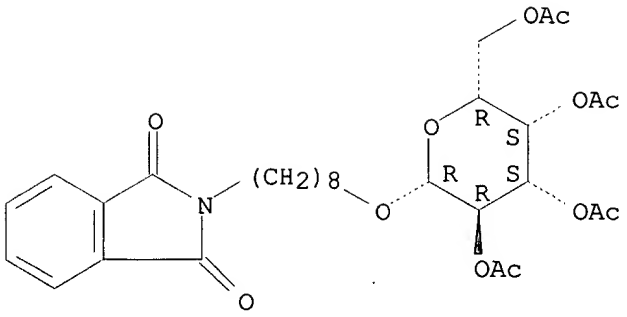
IT **148180-04-5P 148180-10-3P 148180-13-6P**
148180-16-9P 148180-19-2P 148180-22-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and deacetylation of)
RN 148180-04-5 HCAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[8-[(3,4,6-tri-O-acetyl-2-azido-2-deoxy-.beta.-D-mannopyranosyl)oxy]octyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



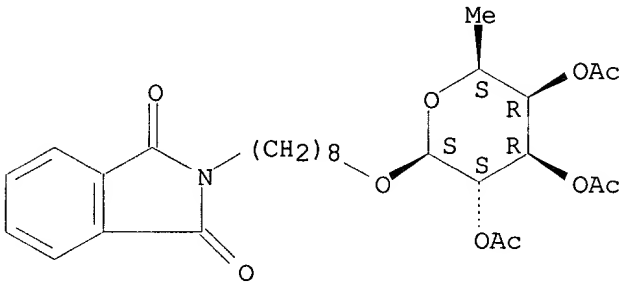
RN 148180-10-3 HCAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[8-[(2,3,4,6-tetra-O-acetyl-.beta.-D-galactopyranosyl)oxy]octyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



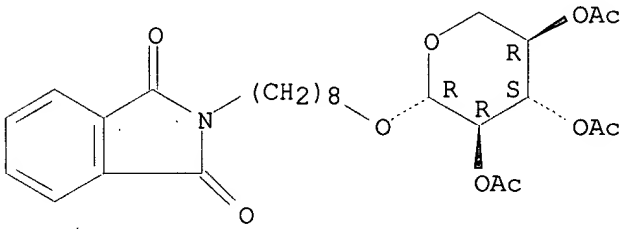
RN 148180-13-6 HCAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[8-[(2,3,4-tri-O-acetyl-6-deoxy-.beta.-L-galactopyranosyl)oxy]octyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



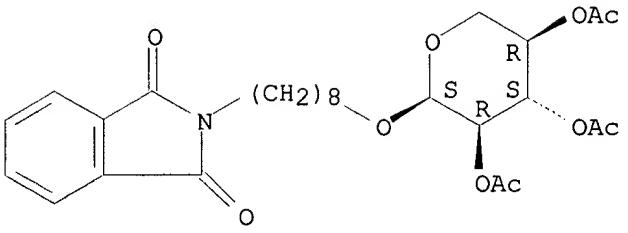
RN 148180-16-9 HCAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[8-[(2,3,4-tri-O-acetyl-.beta.-D-xylopyranosyl)oxy]octyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



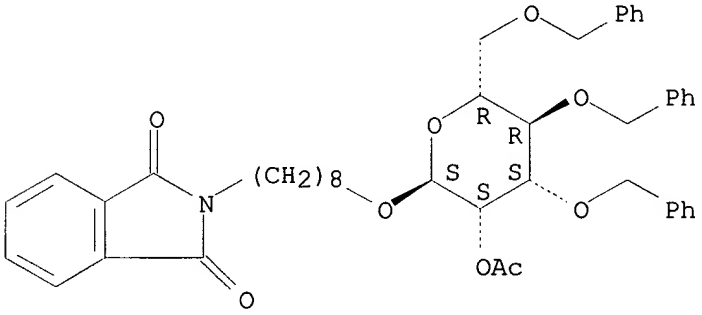
RN 148180-19-2 HCAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[8-[(2,3,4-tri-O-acetyl-.alpha.-D-xylopyranosyl)oxy]octyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



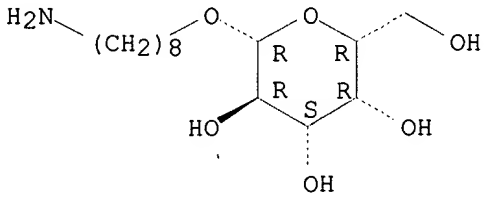
RN 148180-22-7 HCAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[8-[[2-O-acetyl-3,4,6-tris-O-(phenylmethyl)-.alpha.-D-mannopyranosyl]oxy]octyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



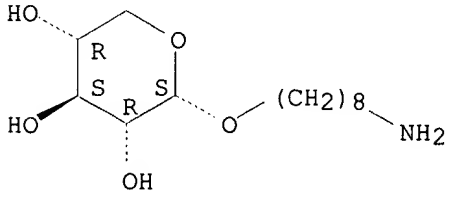
IT **148180-12-5P 148180-21-6P 148180-26-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and glycoconjugate formation of, with polyglutamic acid)
RN 148180-12-5 HCAPLUS
CN .beta.-D-Galactopyranoside, 8-aminooctyl (9CI) (CA INDEX NAME)

Absolute stereochemistry.



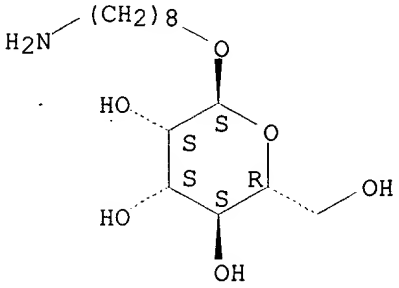
RN 148180-21-6 HCAPLUS
CN .alpha.-D-Xylopyranoside, 8-aminooctyl (9CI) (CA INDEX NAME)

Absolute stereochemistry.



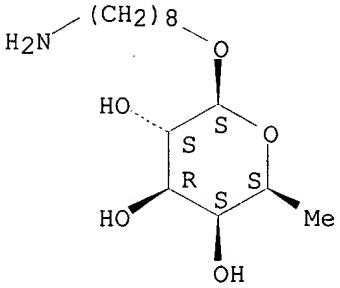
RN 148180-26-1 HCAPLUS
CN .alpha.-D-Mannopyranoside, 8-aminooctyl (9CI) (CA INDEX NAME)

Absolute stereochemistry.



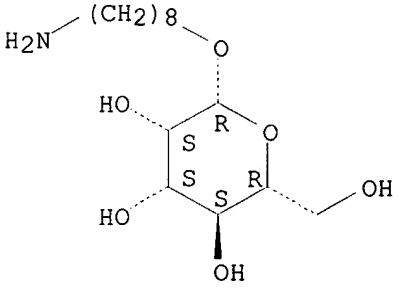
IT **148180-15-8P 148180-29-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and glycoconjugate formation of, with polyglutamic acid)
RN 148180-15-8 HCAPLUS
CN .beta.-L-Galactopyranoside, 8-aminooctyl 6-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

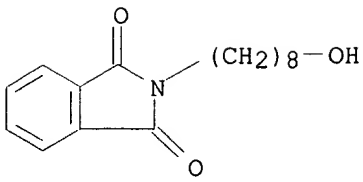


RN 148180-29-4 HCAPLUS
CN .beta.-D-Mannopyranoside, 8-aminooctyl (9CI) (CA INDEX NAME)

Absolute stereochemistry.

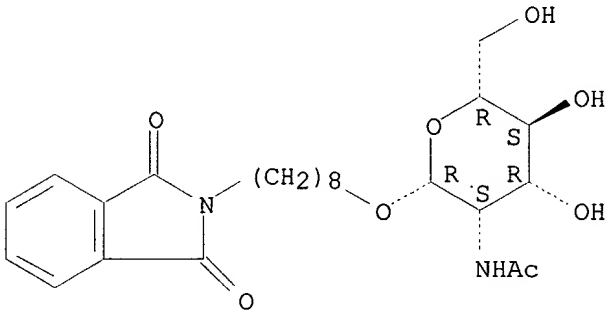


IT **105264-63-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and glycosidation of, with glycopyranosyl halides)
RN 105264-63-9 HCAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-(8-hydroxyoctyl)- (9CI) (CA INDEX NAME)



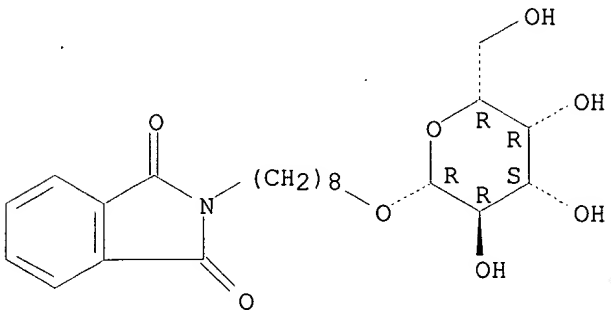
IT **148180-06-7P 148180-11-4P 148180-14-7P**
148180-17-0P 148180-20-5P 148180-23-8P
148180-27-2P 148180-31-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydrazinolysis of)
RN 148180-06-7 HCAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[8-[[2-(acetylamino)-2-deoxy-.beta.-D-mannopyranosyl]oxy]octyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



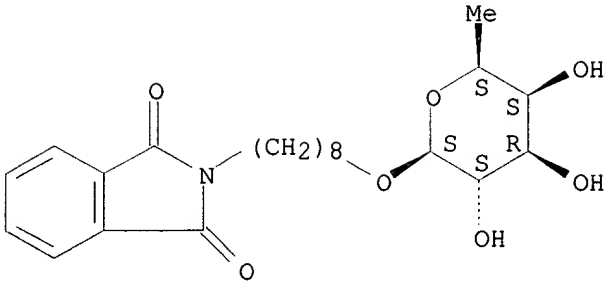
RN 148180-11-4 HCAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[8-(.beta.-D-galactopyranosyloxy)octyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



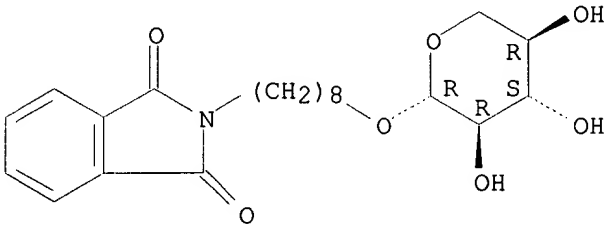
RN 148180-14-7 HCAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[8-[(6-deoxy-.beta.-L-galactopyranosyl)oxy]octyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



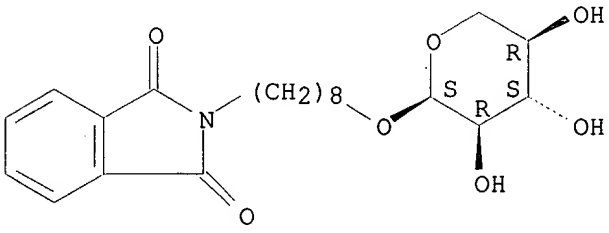
RN 148180-17-0 HCAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[8-(.beta.-D-xylopyranosyloxy)octyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



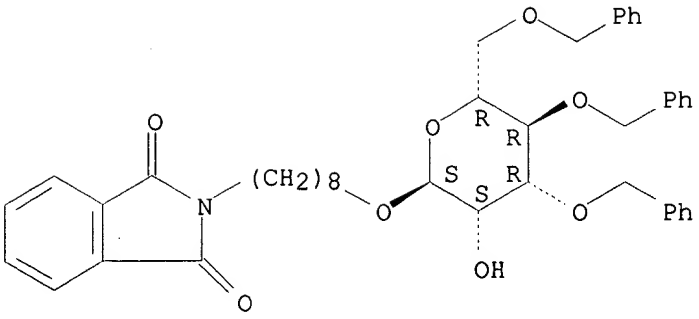
RN 148180-20-5 HCAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[8-(.alpha.-D-xylopyranosyloxy)octyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



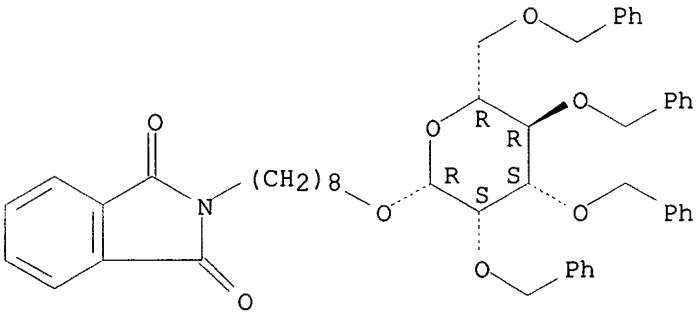
RN 148180-23-8 HCAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[8-[[3,4,6-tris-O-(phenylmethyl)-.alpha.-D-mannopyranosyl]oxy]octyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



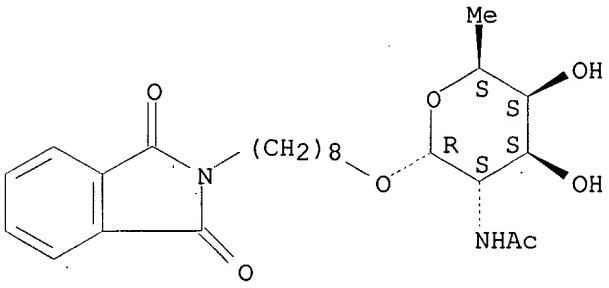
RN 148180-27-2 HCAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[8-[[2,3,4,6-tetrakis-O-(phenylmethyl)-.beta.-D-mannopyranosyl]oxy]octyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



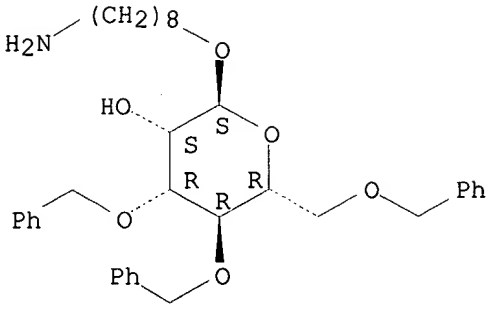
RN 148180-31-8 HCAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[8-[[2-(acetylamino)-2,6-dideoxy-.alpha.-L-galactopyranosyl]oxy]octyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



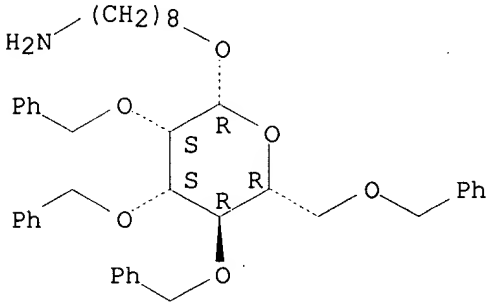
IT **148180-25-0P 148180-28-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydrogenolysis of)
RN 148180-25-0 HCAPLUS
CN .alpha.-D-Mannopyranoside, 8-aminooctyl 3,4,6-tris-O-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



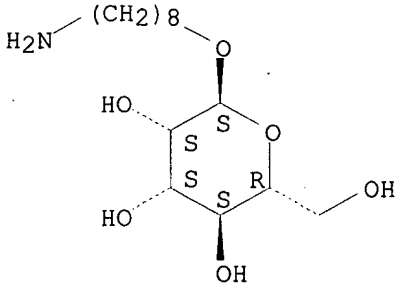
RN 148180-28-3 HCAPLUS
CN .beta.-D-Mannopyranoside, 8-aminooctyl 2,3,4,6-tetrakis-O-(phenylmethyl)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **148180-02-3P 148180-03-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydrolysis of)
RN 148180-02-3 HCAPLUS
CN .alpha.-D-Mannopyranoside, 8-aminooctyl, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

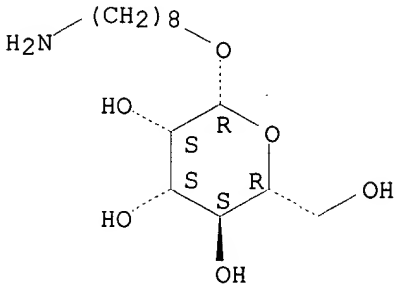


● HCl

RN 148180-03-4 HCAPLUS
CN .beta.-D-Mannopyranoside, 8-aminooctyl, hydrochloride (9CI) (CA INDEX

NAME)

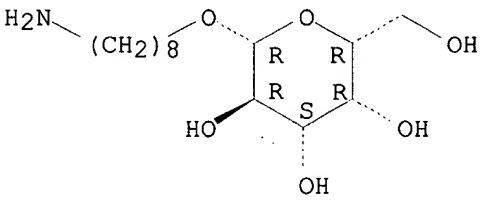
Absolute stereochemistry.



● HCl

IT **148180-12-5DP, conjugate** with poly-L-glutamic acid sodium salt, p-hydroxyphenylethanamide deriv. and 125I-labeled deriv.
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and plasma elimination rate of)
RN 148180-12-5 HCAPLUS
CN .beta.-D-Galactopyranoside, 8-aminooctyl (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **26247-79-0DP**, p-hydroxyphenylethanamide deriv. and 125I-labeled deriv. **148180-15-8DP, conjugate** with poly-L-glutamic acid sodium salt, p-hydroxyphenylethanamide deriv. and 125I-labeled deriv. **148180-21-6DP, conjugate** with poly-L-glutamic acid sodium salt, p-hydroxyphenylethanamide deriv. and 125I-labeled deriv. **148180-26-1DP, conjugate** with poly-L-glutamic acid sodium salt, p-hydroxyphenylethanamide deriv. and 125I-labeled deriv. **148180-29-4DP, conjugate** with poly-L-glutamic acid sodium salt, p-hydroxyphenylethanamide deriv. and 125I-labeled deriv.
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and plasma elimination rate of)
RN 26247-79-0 HCAPLUS
CN L-Glutamic acid, homopolymer, sodium salt (9CI) (CA INDEX NAME)

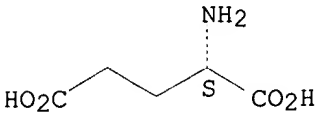
CM 1

CRN 25513-46-6
CMF (C5 H9 N O4)x
CCI PMS

CM 2

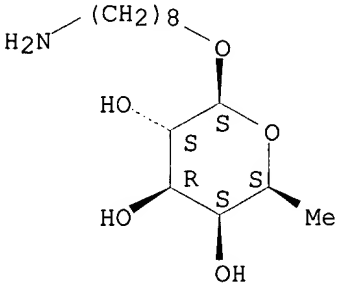
CRN 56-86-0
CMF C5 H9 N O4
CDES 5:L

Absolute stereochemistry.



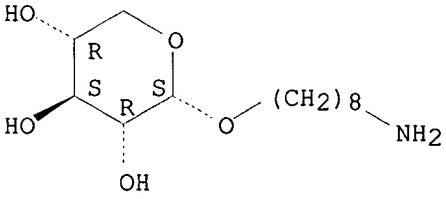
RN 148180-15-8 HCAPLUS
CN .beta.-L-Galactopyranoside, 8-aminooctyl 6-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



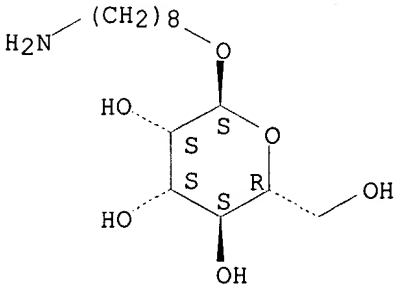
RN 148180-21-6 HCAPLUS
CN .alpha.-D-Xylopyranoside, 8-aminooctyl (9CI) (CA INDEX NAME)

Absolute stereochemistry.



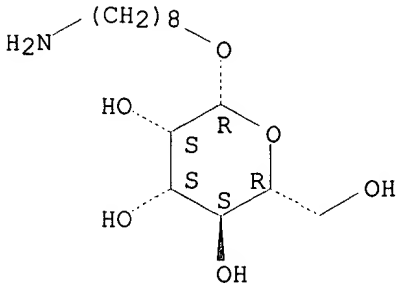
RN 148180-26-1 HCAPLUS
CN .alpha.-D-Mannopyranoside, 8-aminooctyl (9CI) (CA INDEX NAME)

Absolute stereochemistry.



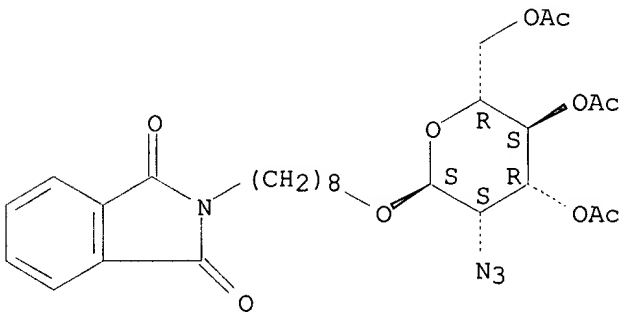
RN 148180-29-4 HCAPLUS
CN .beta.-D-Mannopyranoside, 8-aminooctyl (9CI) (CA INDEX NAME)

Absolute stereochemistry.



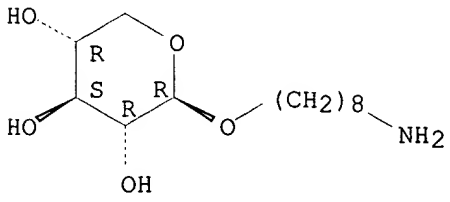
IT **148180-07-8P 148180-18-1P 148180-24-9P**
148180-32-9P 148180-33-0P 148200-40-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 148180-07-8 HCAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[8-[(3,4,6-tri-O-acetyl-2-azido-2-deoxy-.alpha.-D-mannopyranosyl)oxy]octyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



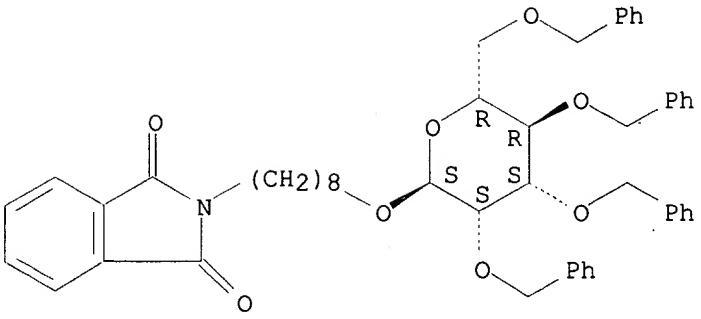
RN 148180-18-1 HCAPLUS
CN .beta.-D-Xylopyranoside, 8-aminooctyl (9CI) (CA INDEX NAME)

Absolute stereochemistry.



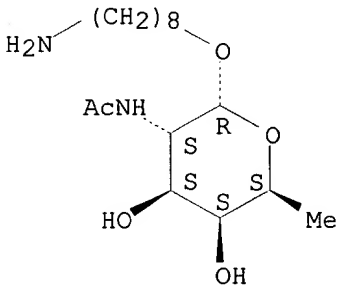
RN 148180-24-9 HCAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[8-[[2,3,4,6-tetrakis-O-(phenylmethyl)-.alpha.-D-mannopyranosyl]oxy]octyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



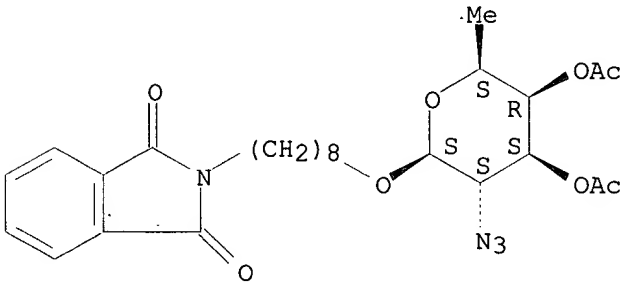
RN 148180-32-9 HCAPLUS
CN .alpha.-L-Galactopyranoside, 8-aminooctyl 2-(acetylamino)-2,6-dideoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



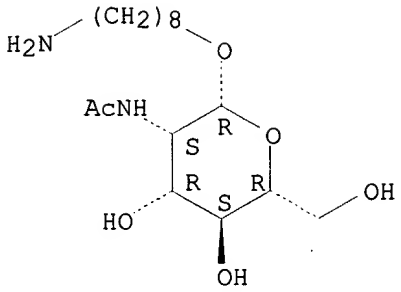
RN 148180-33-0 HCAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[8-[(3,4-di-O-acetyl-2-azido-2,6-dideoxy-.beta.-L-galactopyranosyl)oxy]octyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

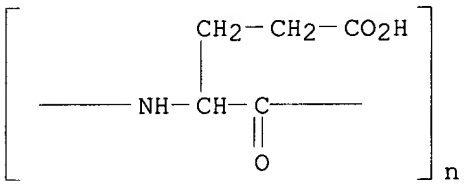


RN 148200-40-2 HCAPLUS
CN .beta.-D-Mannopyranoside, 8-aminooctyl 2-(acetylamino)-2-deoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **24991-23-9P 25513-46-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn., amidation, and glycoconjugate formation of)
RN 24991-23-9 HCAPLUS
CN Poly[imino[(1S)-1-(2-carboxyethyl)-2-oxo-1,2-ethanediyl]] (9CI) (CA INDEX NAME)

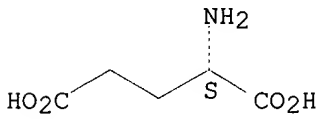


RN 25513-46-6 HCAPLUS
CN L-Glutamic acid, homopolymer (9CI) (CA INDEX NAME)

CM 1

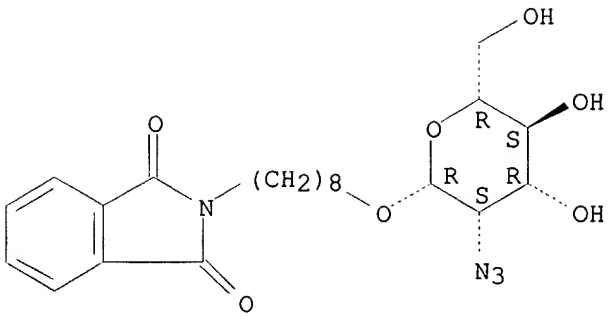
CRN 56-86-0
CMF C5 H9 N O4
CDES 5:L

Absolute stereochemistry.



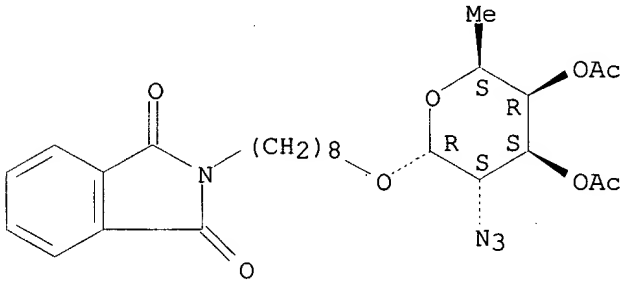
IT **148180-05-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn., borohydride redn., and N-acetylation of)
RN 148180-05-6 HCAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[8-[(2-azido-2-deoxy-.beta.-D-mannopyranosyl)oxy]octyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **148180-30-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn., redn., and N-acetylation of)
RN 148180-30-7 HCAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[8-[(3,4-di-O-acetyl-2-azido-2,6-dideoxy-.alpha.-L-galactopyranosyl)oxy]octyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L13 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:147977 HCAPLUS
DOCUMENT NUMBER: 118:147977
TITLE: Preparation of (carboxymethyl)mannoglucan and derivatives as pharmaceutical carriers targeting cancer cells
INVENTOR(S): **Inoue, Kazuhiro**; Ito, Teruomi; Kawaguchi, Takayuki; Aono, Katsutoshi; Okuno, Satoshi; Yano, Toshiro
PATENT ASSIGNEE(S): Drug Delivery System Institute, Ltd., Japan
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9214759	A1	19920903	WO 1992-JP184	19920221
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
CA 2081025	AA	19920822	CA 1992-2081025	19920221
EP 526649	A1	19930210	EP 1992-905093	19920221

EP 526649	B1	19980520			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
JP 07084481	B4	19950913	JP 1992-504624	19920221	
AT 166361	E	19980615	AT 1992-905093	19920221	
ES 2117664	T3	19980816	ES 1992-905093	19920221	
US 5567690	A	19961022	US 1995-397560	19950302	
US 5863907	A	19990126	US 1996-681981	19960730	
US 5863908	A	19990126	US 1996-689095	19960730	
PRIORITY APPLN. INFO.:			JP 1991-27544	19910221	
			JP 1991-360395	19911227	
			WO 1992-JP184	19920221	
			US 1992-934501	19921021	
			US 1993-136039	19931014	
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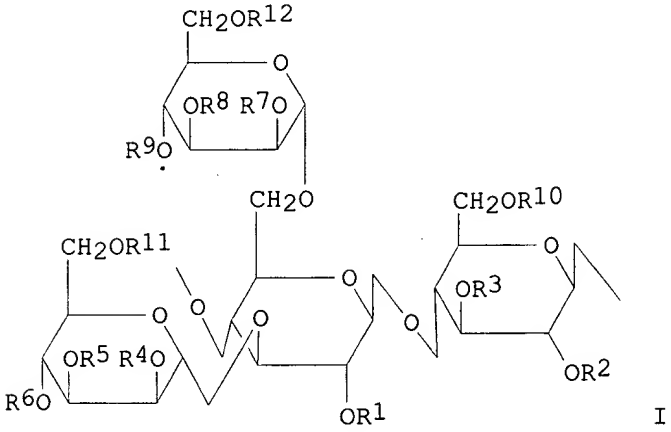
GI



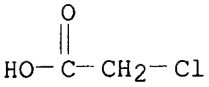
I

AB The title compds. composed of **tetrasaccharide** units (I; R1 - R12 = H, CH2CO2H; wherein part or the whole of the mannopyranose and/or glucopyranose rings of the **tetrasaccharide** units are opened provided that no mannopyranose rings branch off from the opened glucopyranose rings) or their salts [e.g. Pt(NH3)2], increasing the serum life of a pharmaceutical and improving its directivity toward cancer tissue, are prepd. by reacting a mannoglucan composed of I (R1 - R12 = H) with a haloacetic acid. Thus, 20 mL H2O and 1.05 g NaOH were added to 500 mg a mannoglucan of Microellobosporia grisea (manuf. by fermn. given) under cooling, to the resulting clear soln., 1.5 g ClCH2CO2H was added under cooling, and the mixt. was stirred at room temp for 20 h. The reaction liq. was brought to pH 8 with AcOH and poured into 80 mL MeOH to give a white ppt. which was collected, successively washed with MeOH and acetone, and dried in vacuo to give 481 mg (carboxymethyl)mannoglucan with 0.08 degree of substitution. This was labeled by oxidizing with KIO4 in H2O and reducing with tritium-labeled NaBH4 and at 10 mg/kg inoculated to rats transplanted with Walker 256 tumor cells to show the concn. of 19,210 .+-. 630 and 575 .+-. 102 ng/g in the tumor and serum, resp., after 24 h.

IT **79-11-8**, Chloroacetic acid, reactions
RL: RCT (Reactant)
(carboxymethylation by, of mannoglucan)

RN 79-11-8 HCAPLUS

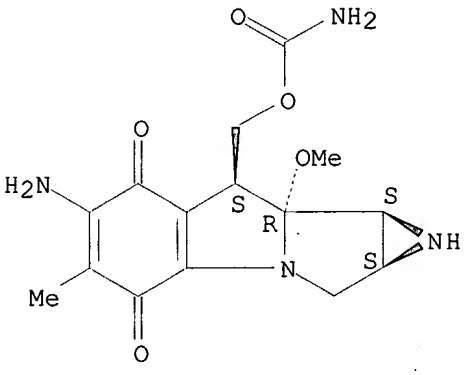
CN Acetic acid, chloro- (8CI, 9CI) (CA INDEX NAME)



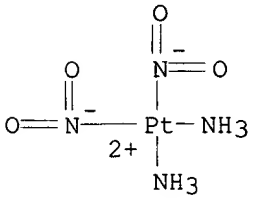
IT **11078-31-2DP**, Mannoglucan, carboxymethyl derivs.
RL: SPN (Synthetic preparation); PREP (Preparation)
(of Microellobosporia grisea , prepn. of, as targeting pharmaceutical carriers)
RN 11078-31-2 HCAPLUS
CN D-Gluco-D-mannan (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **50-07-7DP**, Mitomycin, **conjugate** with mannoglucan
14409-61-1DP, complex with (carboxymethyl)mannoglucan deriv.
20830-81-3DP, Daunorubicin, **conjugate** with mannoglucan deriv.
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of, as antitumor agent)
RN 50-07-7 HCAPLUS
CN Azirino[2',3':3,4]pyrrolo[1,2-a]indole-4,7-dione, 6-amino-8-[[(aminocarbonyl)oxy]methyl]-1,1a,2,8,8a,8b-hexahydro-8a-methoxy-5-methyl-, (1aS,8S,8aR,8bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 14409-61-1 HCAPLUS
CN Platinum, diamminebis(nitrito-.kappa.N)-, (SP-4-2)- (9CI) (CA INDEX NAME)



RN 20830-81-3 HCAPLUS
CN 5,12-Naphthacenedione, 8-acetyl-10-[(3-amino-2,3,6-trideoxy-.alpha.-L-lyxo-hexopyranosyl)oxy]-7,8,9,10-tetrahydro-6,8,11-trihydroxy-1-methoxy-,

(8S,10S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.